Analysis of national HIV treatment guidelines

in 8 countries of Eastern Europe
and Central Asia
and 5 countries of South-Eastern Europe

2020

Team of authors

Sergey Golovin, Aleksey Mikhailov, Tatyana Khan, Nikolay Goloborodko

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The main goal of this document is to contribute to the efforts undertaken by the state authorities of the countries of Eastern Europe and Central Asia, as well as South-Eastern Europe, in the fight against the HIV epidemic. The authors of the report are not responsible for the use and interpretation of the data, conclusions, and recommendations presented in this report by third parties.

The conclusions and recommendations contained in this report reflect the views of the authors, which may not coincide with the views of other stakeholders.

The views expressed in this publication are solely those of the authors and may not reflect the views of the organizations of the consortium and the Global Fund to Fight AIDS, Tuberculosis, and Malaria.

Contents

List of abbreviations

AIDS	acquired immunodeficiency syndrome
AL	albumin
ALT	alanine aminotransferase
ANC	antenatal care (women's consultation)
ART	antiretroviral therapy
ARV	antiretroviral
AST	aspartate aminotransferase
B&H	Bosnia and Herzegovina
BAAR	acid-alcohol resistant bacillus
bid	twice a day
BMI	body mass index
BP	blood pressure
CDD/CDO	consultative and dispensary department/office
CG	clinical guidelines
CHCV	chronic hepatitis C virus
CHE	Center for Hygiene and Epidemiology
CHO	city healthcare organizations
CMV	cytomegalovirus
CNS	central nervous system
CPs	clinical protocols
CSOs	civil society organizations
CSW (SW)	commercial sex workers (sex workers)
CT	computerized tomography
CVD	cardiovascular disease
CXR	chest X-ray
DAAs	direct-acting antivirals
DBS	dried blood spot
DDA	disease-disease association
DHF	district healthcare facility
DOTS	directly observed therapy strategy
DST	drug susceptibility testing
EACS	European AIDS Clinical Society
ECG	electrocardiography
EDL	Essential Drug List
EECA	Eastern Europe and Central Asia
eGFR	estimated glomerular filtration rate
EIDM	early infant diagnosis method
ELISA	enzyme-linked immunosorbent assay
FBC	full blood count

FDCs	fixed-dose combinations
FIs	fusion inhibitors
FL	federal law
FMC	family medicine center
HAND	HIV-associated neurocognitive disorder
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HPTF	healthcare and preventive treatment facility
HSV	herpes simplex virus
IB	immunoblotting (Western blot)
ICA	immune-chemiluminescence assay
IDO	infectious diseases office
IGRA	interferon gamma release assay
INSTIs	integrase strand transfer inhibitors (integrase inhibitors)
IPT	isoniazid preventive therapy
IRIS	immune reconstitution inflammatory syndrome
iv	intravenous
KR	Kyrgyz Republic
MAC	Mycobacterium avium complex
MCT	mother-to-child transmission
MDR-TB/XDR-TB	multidrug/extensively drug-resistant tuberculosis
MDT	multidisciplinary team
mhGAP	WHO Mental Health Gap Action Program
MHSPP	Ministry of Health and Social Protection of the Population
MoH	Ministry of Health
MP	medicinal product
MRI	magnetic resonance imaging
MSM	men who have sex with men
MTCT	mother to child transmission
N/A	not applicable, not applicable
NCP	national clinical protocols
NGOs	non-governmental organizations
NGOs/NPOs	non-governmental/non-profit organizations
NNRTIs	non-nucleoside reverse transcriptase inhibitors
NRTIs	nucleoside (nucleotide) reverse transcriptase inhibitors
NSPs	needle and syringe programs
OECD	Organization for Economic Cooperation and Development
OI	opportunistic infections
OST	opioid substitution therapy
PCR	polymerase chain reaction

PDL	places of deprivation of liberty
PEP	post-exposure prophylaxis
PHC	primary health care
PI/b	boosted protease inhibitors
PITC	provider-initiated HIV testing & counseling
PLCS	pre-labor cesarean section
PLHIV	people living with HIV
PMTCT	prevention of mother-to-child transmission (of HIV)
PPD	purified protein derivative skin test
PrEP	pre-exposure prophylaxis
PWID	people who inject drugs
qd	ones a day
RC AIDS	Regional Center for the Prevention and Control of AIDS
RF	Russian Federation
RK	Republic of Kazakhstan
RM	Republic of Moldova
RNA	ribonucleic acid
RT	rapid test
RT	Republic of Tajikistan
RUz	Republic of Uzbekistan
S&RH	sexual and reproductive health
SSEP	State Service of Execution of Punishment
STIs	sexually transmitted infections
TB	tuberculosis
TBD	TB drugs
TC	testing and counseling
TDM	therapeutic drug monitoring
TGs	transgender
TMP/SMX	trimethoprim/sulfamethoxazole
TST	tuberculin skin test
UN	United Nations
UNAIDS	Joint United Nations Program on HIV/AIDS
UNDP	United Nations Development Program
UNICEF	United Nations Children's Fund,
UNODC	United Nations Office on Drugs and Crime
VCCT	voluntary confidential counseling and testing
VL	viral load
WB	Western blot
WHO	World Health Organization
WR	Wasserman reaction

Drug abbreviations:

3TC	lamivudine
ABC	abacavir
ATV	atazanavir
BIC	bictegravir
COBI/c	cobicistat
d4T	stavudine
DAC	daclatasvir
DDL	didanosine
DOR	doravirin
DRV	darunavir
DTG	dolutegravir
EFV	efavirenz
EFV400	efavirenz at 400 mg
ETR	etravirine
FOS	fosamprenavir
FTC	emtricitabine
G/P	glecaprevir/pibrentasvir
IDV	indinavir
LPV/r	lopinavir/ritonavir
MVC	maraviroc
NFV	nelfinavir
NVP	nevirapine
pAZT	phosphonate azidothymidine
PrOD	paritaprevir/ritonavir/ombitasvir and dasabuvir
RAL	raltegravir
RBV	ribavirin
RTV/r	ritonavir
SOF	sofosbuvir
SOF/LED	sofosbuvir/ledipasvir
SOF/VEL	sofosbuvir/velpatasvir
SQV	saquinavir
TDF	tenofovir disoproxil fumarate
TLD	tenofovir/lamivudine/dolutegravir
TLE	tenofovir/lamivudine/efavirenz
ZDV (AZT)	zidovudine (azidothymidine)

Introduction

According to the Joint United Nations Program on HIV/AIDS (UNAIDS), the HIV epidemic in Eastern Europe and Central Asia (EECA) continues to grow. The EECA region as a whole is far from reaching the 90-90-90 targets. Only about 38% of the total estimated people living with HIV in the EECA region have access to antiretroviral therapy in 2018. In absolute terms, this is about 650 000 people. At the same time, over a million people, as of 2018, did not receive ART. Thus, the governments of the countries in the region face several important tasks in terms of counteracting HIV infection. On the one hand, it is necessary to significantly increase the number of people included in HIV treatment programs. On the other hand, modern HIV therapy standards are constantly being revised following new clinical options, as well as new information collected about the use of drugs that are already on the market. In particular, the World Health Organization (WHO) in 2018 revised the first-line treatment standards for HIV infection, including the DTG integrase inhibitor and a reduced dosage of the non-nucleoside reverse transcriptase inhibitor EFV (400 mg). Many of the countries in the region are recipients of the Global Fund's financial resources allocated to various sections of HIV prevention and treatment, that is why countries harmonize their national clinical guidelines with the recommendations of WHO (as one of the UN agencies). This agreement is not a formal requirement, but it provides an opportunity for countries of the region to harmonize their national recommendations with the minimum standards laid down in the WHO guidelines, and it can contribute to the development of a coordinated advocacy strategy for access to treatment in the region.

Due to regular changes in international standards, it is extremely important to understand what principles are used to treat HIV-positive people at the country level, how these standards are regulated, what is the procedure for their revision, and so on.

As a rule, standards and algorithms for the HIV infection treatment (as well as for other diseases) are prescribed in national clinical guidelines or protocols. The National Clinical Guidelines is the document that is the basis for clinicians in a country to make decisions about how to treat, care, and support patients. These documents describe such key topics as algorithms for making a diagnosis, prescribing therapy, choosing the first-line and subsequent treatment regimens, considering the patient's characteristics, choosing therapy for concomitant diseases, taking into account drug interactions, and the patient's condition, monitoring during therapy, and so on. Treatment recommendations can be mandatory (in this case, they are issued by a specialized department, most often by the Ministry of Health, in the form of an order) or they can be advisory (as implied by the term). As a rule, the authors of the national recommendations are professional associations or specially created working groups of specialists at the country level.

In theory, clinical guidelines (or protocols) are documents that should have an impact not only on the clinical but also on the economic aspects of responding to the epidemic. Specialists responsible for budgeting and procurement of drugs and test kits should form the need for drug therapy and reagents, inter alia based on recommendations. According to the initial assessment, agencies responsible for liaison with suppliers should initiate, if necessary, negotiations for price reductions, if the required volume of clinically important drugs and test kits cannot be provided within the current budget and opportunities for budget expansion is limited.

In other words, in theory, the clinical guidelines should be the fundamental document for the formation of the nomenclature of purchased drugs and medical devices, namely, largely guided by the recommendations written by subject matter experts, governments should choose what exactly and in what volumes they will purchase. Therefore, the content of the clinical guidelines is critical.

To prepare this report, we formulated several hypotheses. First, each of the 13 countries included in the analysis has national clinical guidelines, or instead, they use the clinical guidelines produced by the World Health Organization (WHO) and the European AIDS Clinical Society (EACS). Second, this document is publicly available so that it can be analyzed and compared with applicable international standards. Third, the clinical aspects of countering the epidemic (for example, the choice of drugs) in these 13 countries can be regulated, in addition to recommendations, by other documents.

The purpose of this report is to provide **recommendations on how to optimize national standards for HIV treatment in EECA and South-Eastern Europe, and standards for HIV treatment in the countries included in the analysis.** The analysis was mainly focused on the texts of national clinical guidelines for the treatment of HIV infection, but in some cases, it also covers other relevant documents, such as restrictive lists, lists of purchased drugs, certain recommendations on prevention and other documents that somehow regulate case-management of HIV positive people.

Optimization options were developed based on the analysis of the texts of the recommendations and other documents carried out by country experts using a pre-developed methodology. The WHO Guidelines were chosen as the benchmark for comparative analysis as the minimum generally accepted standard to form recommendations for HIV treatment from a public health perspective.

It should be clarified that options for optimizing national standards of HIV treatment were based mainly on the opinion of the national experts who conducted the analysis. Accordingly, the authors of the report propose to use them as the foundation for further discussions on updating national clinical guidelines and other applicable regulatory documents.

Methodology and structure of the report

The report contains summary information on 8 countries of Eastern Europe and Central Asia (EECA) (Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russian Federation, Tajikistan, Uzbekistan) and 5 countries of South-Eastern Europe (Bosnia and Herzegovina, Romania, North Macedonia, Serbia, Montenegro).

These EECA countries are in the focus of research and activities under the project titled "Sustainability of Services for Key Populations in the Eastern Europe and Central Asia Region (SoS_project)" as eligible for support from the Global Fund, which is determined by the income level according to the World Bank classification and the incidence rate, according to compliance with the Global Fund to Fight AIDS, Tuberculosis, and Malaria Policy.

According to 2019 estimates, the EECA region is the only region in the world where there is a constant increase in the incidence of HIV infection[1]. Most PLHIV in the EECA region lives in the following nine countries: Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Ukraine, Tajikistan, and Uzbekistan. The Russian Federation is the main driver of new HIV infections in the EECA region both in terms of prevalence (total number of PLHIV) and incidence (number of new HIV infections). To meet the need for access to treatment, provided the growth of PLHIV in these countries, as well as to achieve the global 90-90-90 targets, it is critical to optimize treatment regimens according to the latest WHO guidelines.

In 2019, at the request of partners and based on the growing incidence rate, within the SoS_ project, it was decided to expand the activities by adding 5 countries of South-Eastern Europe to optimize treatment regimens, including WHO guidelines.

A specially developed form was used to analyze the recommendations. It consisted of several parts, namely:

- Basic information (document availability, current edition, name, link, legal status, frequency of revision, level of evidence, list of documents that additionally regulate the clinical aspects of countering the HIV epidemic)
- Diagnostic recommendations
- ARV drugs for HIV prevention
- Antiretroviral therapy regimens
- Prevention and treatment of concomitant infections and diseases
- Health service delivery
- Other clinically significant discrepancies that do not fall within the above blocks.

The form consisted of three basic columns: 1) an extract from the national guidelines; 2) an expert's comment; 3) an extract from the relevant section of the WHO guidelines. Taking into account the specifics of this project, the 2016 edition[2] of the World Health Organization's (WHO) Guidelines was taken as a basis, considering updates in 2018[3] and 2019[4] regarding the prescription of antiretroviral drugs.

1 https://www.avert.org/hiv-and-aids-eastern-europe-central-asia-overview
2 https://www.who.int/hiv/pub/arv/arv-2016/ru/
3 https://www.who.int/hiv/pub/guidelines/ARV2018update/en/
4 https://apps.who.int/iris/bitstream/handle/10665/325892/WHO-CDS-HIV-19.15-eng.pdf

National specialists in the field of HIV infection contributed to the analysis. Minimum requirements: higher medical education, clinical experience in the field of infectious diseases for at least 5 years, experience in administrative work in the healthcare sector, good knowledge of the legal framework regulating clinical aspects of the fight with HIV- infection.

The report is structured as follows: after the introduction and methodology, there are brief descriptions of the main findings and recommendations for each of the 13 countries included in the analysis. Basically, brief descriptions present those items that, according to country experts, need to be adjusted, taking into account the recommendations of WHO or other international recommendations. As far as possible, the comments are grouped according to thematic blocks of which the questionnaire form consisted.

Following the country briefs, general conclusions and recommendations for the analysis are provided. Annex 1 contains the titles of the main analyzed documents in each country and links to them (if the documents are publicly available online). Annex 2 contains detailed country profiles. They are presented in the form of tables completed by country experts according to the methodology.

Belarus

The clinical protocol “Diagnosis and treatment of patients with HIV infection” (CP HIV 2017) was taken as the basis for the analysis in Belarus. This document regulates most of the issues considered in the WHO guidelines. At the same time, the protocol does not regulate a number of issues from the WHO guidelines, including PEP and PrEP, some issues of how programs and services are managed, procedural issues of creation, dissemination, and evaluation of recommendations.

The authors (developers) are not indicated in the CP HIV 2017, it is unclear whether the text of the protocol is the result of their joint discussion or simply each of the authors wrote their own part. The creation of clinical protocols approved by the MoH does not involve the participation of public/patient-led organizations; only healthcare workers develop and review them.

The CP HIV 2017 does not describe the development procedure, including the regulation of conflicts of interest, the main sources of information used (including no reference to the 2016 WHO Guidelines, which were the main source for the development of the protocol), methods of evidence synthesis and a system of evidence quality assessment, procedures for resolving disputes and an independent expert assessment (despite the fact that it was probably carried out - all clinical protocols approved by the MoH go through an external expert assessment system).

The CP HIV 2017 does not define the format for presenting recommendations, does not indicate the level of evidence and strength of individual recommendations. The option of revising the recommendations is not provided, and their regularity (their likely time frame of revision) and the procedure are not defined.

There is no summary of the recommendations with a breakdown into new and previous ones (not modified, or revised and updated in the current protocol); provisions of good practice are not formulated.

In general, the national clinical protocol (CP HIV 2017) complies with the 2016 WHO Guidelines. In particular, the 2017 clinical protocol has already declared universal access to ART in the Republic of Belarus since 01 January 2018 (CP HIV 2017, article 6.1), but, in reality, it started in mid-2017. Taking into account the staging of the transition from the previous recommendations to universal access, the priority of providing ART for certain categories of PLHIV was declared (which generally corresponded to those in the WHO 2016 Guidelines, first of all, identifying people with the progression of HIV infection according to the clinical picture up to 3-4 stages and reducing the level of CD4 lymphocytes to the level of advanced immunodeficiency), and ART is currently provided to all PLHIV.

At the same time, due to amendments in the WHO Guidelines from 2017 to 2019 and taking into account the identified number of inconsistencies and gaps in regulation, the national health authorities of Belarus should be recommended to harmonize national protocols, bringing them in line with the current WHO guidelines according to the paragraphs noted below (see Annex 2).

Key Points

Diagnostics

A general comment in the CP HIV 2017 regarding the diagnosis is associated **with the long chain from test to treatment due to limitations** in the use of laboratory tests, the involvement of an excessive number of specialists (different people provide pre-test counseling during testing, reporting the test result, conducting epidemiological studies and subsequent provision of medical care), and **there are no plans to reduce the testing chain for key populations.** According to the CP HIV 2017, rapid testing (RT) **is possible only with the use of rapid blood tests, but not for saliva** - WHO does not impose such restrictions. The result of RT is regarded as primary positive only if it was obtained "during the blood count in a healthcare facility" with its obligatory fixation "in the patient's medical records", and the "healthcare facility" also sends the second (taken again) blood sample to the arbitration laboratory. This contradicts the 2016 WHO Guidelines that "trained lay health workers, under specialist supervision, can conduct safe and effective HIV testing on their own using rapid diagnostic tests."

WHO good practice provision, namely "finger stick sampling for sample preparation may be supervised by trained non-laboratory personnel," is also **not implemented.** In other words, at the level of recommendations, NGOs are excluded from the testing process, which is a barrier in the chain from examination to treatment. In reality, NGOs perform RT using saliva, but they are not recognized by the healthcare system as a primary HIV test (which makes the testing chain longer), or NGOs hire healthcare workers to conduct finger sticks sampling from clients to provide RT for blood (which increases the cost of low-threshold care).

From now on, it is important to note that there are updated 2019 WHO Guidelines on the testing algorithm, comparison with which was not included in the terms of reference. This is an additional area of research.

ARV drugs for the prevention of HIV infection

The protocol does not contain regulation related to the use of PEP and PrEP.

Antiretroviral therapy regimens

The protocol does not recommend the use of DTG and EFV400 in first-line regimens, either in preferred or alternative ones. DTG is designated as acceptable if other drugs cannot be used due to virus resistance or toxicity. The dosage of EFV is not prescribed in the treatment regimens, although dosages of 600 and 400 mg are mentioned. Including DTG in the preferred first-line regimens is limited by patent protection for drugs in Belarus and their related high price (2 160 USD for yearly treatment course with DTG compared to 36 USD for a yearly course with EFV600 in 2018).

Approaches to changing the ART regimen in case of its ineffectiveness in Belarus are generally in line with the 2016 WHO Guidelines.

Among the barriers that are not directly related to the CP HIV 2017 are the followings:

- EFV400 and RAL are not registered in Belarus;

- It is impossible to import a generic version of DRV/r in the form of a thermo-stable FDC due to the patent protection of a thermo-stable RTV;
- The CP HIV 2017 recommends to use “combined MP in fixed dosage and [regimens] with the least number of intakes per day”, but in reality, some non-combined NRTIs (ABC + 3TC) are used, and the proportion of “3 in 1” combinations for 2017- 2018 was no more than 5% of all regiments.

Prevention and treatment of concomitant infections and diseases

The management of patients with tuberculosis and viral hepatitis is regulated by separate clinical protocols. WHO-recommended inclusion of “assessment and management of depression” in the package of services for all PLHIV is not mentioned in the CP HIV 2017; it is defined only as a contraindication to the use of EFV “in patients with severe mental disorders, depression”.

Health service delivery

The CP HIV 2017 does not define the importance of comprehensive care and the involvement of patient communities in the provision of services, as well as it does not prescribe the specific needs for healthcare services of the main key populations (the CP HIV 2017 defines them as PWID, MSM and TG, female CSW, persons in PDL, and migrants).

Bosnia and Herzegovina

The version of the clinical guidelines that were considered in the study dates to 2016 and is entitled "Clinical Guidelines for HIV/AIDS Treatment" (Sarajevo, 2016). The Guidelines are mentioned in the Strategy for Response to HIV/AIDS in Bosnia and Herzegovina 2011-2016, which was adopted by the Council of Ministers. **However, they are not binding.**

The guidelines should be revised every 3-4 years, and the next revision is scheduled for 2020. The editorial board includes representatives from the Ministry of Health of Bosnia and Herzegovina, the Ministry of Health of the Republic of Srpska, the United Nations Development Program, the Global Fund to Fight AIDS, Tuberculosis, and Malaria, and two non-governmental organizations: Partnership for Health and SIDA.

In general, as the expert notes, "Clinical guidelines for HIV/AIDS Treatment" are in line with the 2016 WHO Guidelines. A revision of clinical guidelines and the protocol for HIV counseling and testing is scheduled for 2020.

Key Points

Diagnostics

The expert has not found any critical discrepancies between the Diagnostics section and the guidelines. However, as it was mentioned above, the new 2019 WHO Guidelines for the testing algorithm should be considered, in particular regarding the Western Blot use. Community-based testing is not provided for by the protocol, which **is not in line with the guidelines.**

ARV drugs for HIV prevention

Clinical protocols include sections on pre- and post-exposure prevention of the HIV infection. The recommended PrEP regimen is TDF/FTC. According to the information received from the country expert, PrEP is used only for MSM. If this is the case, then this practice **does not fully correlate** with the 2016 WHO Guidelines, which state that PrEP is advisable for people at significant risk of infection and is not limited to a specific population.

The recommended control panel circuits are TDF/FTC (or ZDV/3TC) + LPV/r (or RAL).

Antiretroviral therapy regimens

Combinations are included in the preferred treatment regimens. According to the expert's information, the following combinations are available in the country: TDF/FTC, ABC/3TC, and ZDV/3TC.

Among significant aspects regarding the choice of ARV drugs, **the lack of DTG and EFV in a dose of 400 mg in the current version of the guidelines** should be emphasized. These drugs are not available on the Bosnia and Herzegovina market as of 2019. DTG and BIC/TAF/FTC integrase inhibitors are going to be included in the new version of the document. According to the expert, DTG will become available in the country in 2020.

In general, the guidelines **are based on the 2013 WHO regimens, as well as the 2015 DHHS and EACS,** and they need to be adjusted in accordance with the latest revisions of these documents.

Prevention and treatment of concomitant infections and diseases

The protocol contains sections on the management of several co-morbidities in case of HIV infection, including TB, viral hepatitis, cardiovascular disease, and depression.

Health service delivery

The expert noted the decentralized nature of the HIV service provision.

Other

The following barriers and obstacles to full access to treatment were emphasized:

- A complicated process of registering and including preparations in the Essential Medicines List, which is used for establishing the nomenclature at the expense of the mandatory insurance fund;
- High prices for some antiretroviral medicines;
- Some manufacturers are not present on the Bosnia and Herzegovina market.

Georgia

In Georgia, the standards for HIV treatment and care are defined by the Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV infection, adopted in 2018.

According to the ministerial decree on the development of national guidelines for clinical practice N94/n of March 27, 2006, this is the main document for the clinical management of HIV infection in accordance with the principles of evidence-based medicine. The document does not indicate its legal status (mandatory or recommendatory), but it forms the basis for the national program for HIV treatment, including the procurement of ARV drugs.

The 2018 version is an updated version of 2017. This was a partial revision that affected the choice of first-line ART regimens in adults, the remaining chapters remained unchanged, generally in line with the 2016 WHO Guidelines. Certain aspects that are not covered by the 2016 WHO Guidelines were adapted from the US EACS 9.0 and DHHS guidelines for HIV treatment in children.

The guidelines are revised every three years or more often if new evidence becomes available. The revision of the current version is scheduled to be completed in 2020.

The 2018 National Guidelines were developed by a team of 8 experts in healthcare, health systems, public health, laboratory services, and a community representative.

Key Points

Diagnostics

Diagnostic issues are not included in national HIV treatment guidelines, but they are mentioned in national HIV surveillance regulations. In individuals aged 18 months and older, HIV diagnosis is based on an antibody test - a screening test (rapid HIV test or ELISA test) followed by confirmatory testing (Western blot or, in special cases, nucleic acid test).

In accordance with national guidelines for HIV surveillance, post-test counseling is also mandatory for all HIV-positive patients. Pre-test counseling is not required in case of HIV testing for blood donors and pregnant women. All other groups of the population, including those who are being tested based on community organizations or other healthcare facilities, should receive pre- and post-test counseling. The procedure for such counseling is detailed in the HIV surveillance regulations. The instructions specify how to conduct counseling, what information to collect, and how to refer people to the appropriate services.

The current guidelines **do not provide specific guidelines for HIV testing outside of healthcare facilities** (e.g. at community-based organizations). At the same time, there is no regulatory act that prohibits non-healthcare workers from providing HIV testing services. I**n practice, testing is widely available in healthcare facilities and community-based organizations, including through express diagnostics.** However, the inclusion of the WHO guidelines on this issue would be useful to further promote the adoption of community-based HIV testing, including outreach-testing.

ARV drugs for HIV prevention

Recommendations for PrEP are given in the Pre-Exposure Prophylaxis section, according to which it is necessary to offer oral prophylaxis with TDF to people at significant risk of HIV infection as part of a combined HIV prevention approach. PrEP recommendations are **fully consistent** with the 2016 WHO protocols and also provide clear instructions for the management of people on PrEP.

The guidelines also include a section on post-exposure prophylaxis. **The primary preferred PEP regimens for adults and adolescents are TDF + 3TC (or FTC), which is in line with the 2016 WHO Guidelines.** LPV/r or ATV/r is indicated as a preferred third preparation. Where possible, RAL, DRV/r or EFV may be considered as alternatives.

The main preferred PEP regimens for children are AZT + 3TC, and LPV/r is recommended as the third preferred third drug. Alternative third drugs are ATV/r, RAL, DRV, EFV, and NVP.

The 2020 National HIV Program regarding PEP **is developed in accordance with the 2018 WHO** Interim Guidelines, which mentions DTG as the preferred third drug for PEP. This recommendation will be used in national HIV treatment guidelines after revision in 2020.

Antiretroviral therapy regimens

The TDF + 3TC (FTC) + DTG regimen was included national HIV treatment guidelines in Georgia **as the preferred first-line regimen in adults** even before the official 2018 WHO Guidelines were published.

The choice of alternative regimens is in line with the 2016 Guidelines with minor differences –WHO prioritizes EFV400 mg, while national guidelines include both EFV400 mg and EFV600 mg (EFV400 mg is included in first-line alternative regimens for adolescents). Moreover, national guidelines consider **NVP as a 4th alternative drug** if DTG or EFV cannot be prescribed, **while WHO recommends RAL for special circumstances.**

The choice of first-line ART for adolescents in the national guidelines remained the same as in the 2016 WHO Guidelines, largely due to the lack of evidence of DTG use in this patient population at the time of the revision of the guidelines. Along with other new recommendations, this one was taken into account in the national HIV response program and will be officially included in the updated guidelines in 2020.

National HIV treatment guidelines do not contain specific references to combined drugs; this and other aspects of service delivery are defined in the national HIV program. Thus, the procurement of ARVs in 2020 **includes such combined drugs as TDF/3TC/DTG and TDF/FTC/EFV.**

The switching to second- and third-line regimens is carried out after the drug resistance test, which has been available in the country since 2005. Second-line regimens are selected based on drug resistance test results from available drug classes. LPV/r and ATV/r are preferred to PI, DTG is preferred to INSTI. DRV/r, RAL, and ETV are the drugs of choice for third-line treatment regimens.

If the drug resistance test cannot be performed, the choice of second-line drugs is based on previous treatment experience and in accordance with the 2016 WHO Guidelines regarding the switching to second- and third-line regimens. **This part of the national guidelines should be updated in line with the 2019 WHO Guidelines on the switching to second- and third-line regimens.**

Stavudine was stopped using in Georgia after the revision of national guidelines in 2007; the drug has not been used in clinical practice for at least 11 years.

Prevention and treatment of concomitant infections and diseases

The national guidelines fully cover the treatment of co-infections and co-morbidities, **exceeding the standards proposed by WHO.**

The prevention and treatment of non-communicable diseases are part of the core package of services. Specific recommendations include assessment while admission to HIV treatment and ongoing monitoring according to standard protocols developed for the general population. This includes the monitoring of cardiovascular disease, kidney function, diabetes, bone health, cancer screening, cognitive function, and depression.

Health service delivery

The Service Delivery section **is not included** in the guidelines because it goes beyond the requirements for clinical practice guidelines. Service delivery issues are included in the national strategic plan and national HIV program.

Other

The national guidelines do not define adolescents as a separate population group, since the national guidelines apply to all age categories, as epidemiological data show that adolescents in Georgia constitute only a small proportion of PLHIV.

Kazakhstan

The country uses the 2017 Clinical Protocol for the HIV Diagnosis and Treatment of HIV Infection in Adults, approved by the Joint Commission on the Quality of Medical Services of the Ministry of Health of the Republic of Kazakhstan. The protocol is recommendatory. The list of documents additionally regulating the use of ARV drugs in the country is included in Annex 2. Representatives of NGOs do not participate in the editorial board, however, before approval, the draft protocol is posted on a special portal named “Open regulatory legal acts” for discussion with the public, associations and non-governmental organizations.

National guidelines for the diagnosis and treatment of HIV infection in terms of general information correspond to the 2016 WHO Guidelines and are updated in a timely manner (once every 2 years). To date, draft new CPs for the HIV diagnosis and treatment in adults and children have been developed. As of the end of December 2019, the protocols were sent to the MoH of RK for approval.

Key Points

Diagnostics

The national protocol **does not have a recommendation for retesting prior to inclusion in care and treatment programs.** However, with the existing algorithm for HIV diagnosing in the Republic of Kazakhstan (two levels of screening using ELISA testing after a positive first result, confirmation by western blot test and the obligatory provision of an ID document upon delivery of biological material), there is no need to re-test for HIV before being included in care and treatment programs.

A recommendation on the sensitivity and specificity of tests for the diagnosis of HIV infection in children and infants is not included. It is necessary to make recommendations for the draft of a new CP and the approved algorithms regarding the sensitivity and specificity of the tests since the specificity and sensitivity of the tests used are clinically significant for the quality of the studies.

There is no recommendation for testing adolescents; it can be assumed that it is impossible in RK to conduct self-testing for children and adolescents under 18 years old without the consent of parents or guardians. It is necessary to assess the legal framework and develop recommendations for testing adolescents in RK.

The diagnostic algorithms do not comply with the 2019 WHO Guidelines regarding the use of the western blot method for confirmation. It is not clinically significant with the current algorithm. Considering the rating of RK in terms of gross national income per capita, it is recommended to study the experience and algorithms of HIV diagnostics in the OECD (Organization for Economic Cooperation and Development) countries, to analyze all the negative and positive aspects related to HIV diagnostics. The most acceptable version of the algorithm in RK should be developed and implemented based on the analysis results.

ARV drugs for HIV prevention

Pre-exposure prophylaxis of HIV infection is not included in the guidelines. A clinically significant difference in the 2016 WHO Guidelines are recommended for inclusion in the new draft CP.

Algorithm and regiments of PEP for different populations, including PMTCT, are included in the protocols but do not correspond to the latest PEP regimens of WHO as of 2018; it is recommended to amend the new CP according to the WHO guidelines.

Antiretroviral therapy regimens

CP includes the use of DTG and EFV400 according to updated guidelines (2018, 2019) but is part of alternative treatment regimens. It is recommended to include [them] in preferred treatment regimens according to the 2019 WHO Guidelines. This discrepancy is clinically significant, given that these drugs have a more favorable toxicity profile, and DTG also has a high barrier to the development of resistance.

The CP does not have recommendations regarding the use of DTG in women of fertile age and pregnant women; this should be mentioned in the new CP, as this recommendation is clinically relevant. Every woman of fertile age should be informed of all the risks associated with DTG use.

There is first-line ART for special patient groups; this does not meet the WHO guidelines; the new CP needs to be amended.

Prevention and treatment of concomitant infections and diseases

The protocol contains a section on the prevention of HIV-associated diseases. **There is no section on the treatment of the relevant non-communicable diseases in the CP of RK.** It is recommended to study the recommendations of WHO, EACS, DHHS on the prevention and treatment of relevant non-communicable diseases, to adapt and include them in the draft of a new CP. It is clinically significant during the management of HIV-positive patients, since ART regimens, the differential diagnosis of concomitant and concomitant diseases in PLHIV depend on this.

Health service delivery

The CP of RK does not have a section related to this area. Taking into account the distance between the patient's place of residence and the location of the RC AIDS, and the list of limited medical services provided at the RC AIDS level, it is recommended to study and consider the issue of decentralization of services for PLHIV in RK.

Kyrgyzstan

Separate legislative acts regulate access to HIV treatment in Kyrgyzstan (see Annex 2, a detailed country profile).

HIV treatment is given based on the document “Clinical Protocols on HIV Infection for Outpatient and Inpatient Levels of Health Care” as of 2017. Revision of clinical protocols is carried out as fundamentally new data become available. While developing current treatment protocols, the editorial board also included representatives of public and international organizations. They were among the initiators of the revision of the recommendations in 2017 and 2019 and they participated in the meetings of the working groups on drafting new protocols, making, among other things, proposals for optimizing antiretroviral therapy regimens (including the inclusion of dolutegravir in therapy standards) . Kyrgyzstan's experience regarding the involvement of the patient community’s representatives to develop recommendations for HIV treatment takes into account international practice and should be adapted in other EECA countries where this practice has not yet been fully implemented.

The revision of the Clinical Protocols on HIV Infection is currently being finalized to consider the updated 2018 and 2019 WHO Guidelines.

Key Points

Diagnostics

Repeated testing before ART and the introduction of rapid tests are not included in CP, but in addition to CP, the instruction titled "Laboratory Diagnosis of HIV Infection in the Kyrgyz Republic" was developed, approved by the order of the Ministry of Health of the Kyrgyz Republic No. 303 dated of April 28, 2018. Rapid tests are used in healthcare and non-healthcare facilities, including NGOs. RT is carried out only by specialists who have specially trained and received an appropriate certificate.

ARV drugs for HIV prevention

Within the comprehensive HIV prevention measures, people with an increased risk of HIV infection are recommended to use ARV drugs containing TDF for pre-exposure prophylaxis, **which is in line with the 2016 WHO Guidelines.**

Antiretroviral therapy regimens

The 2016 WHO Guidelines on ART are mentioned in CP, but there are some discrepancies, in particular, there is no recommendation for the use of combination drugs. In real practice, combination drugs are used in the first-line ART in most cases, with the exception of cases of drug intolerance in patients. The main combination ARVs that are in use are listed in the EDL and procured (EFV/FTC/TDF; FTC/TDF; ABC/3TC; 3TC/AZT).

DTG and EFV400 are prescribed in CP in alternative ART regimens. The lack of DTG in preferred first-line regimens does not take into account the updated 2018 and 2019 WHO Guidelines.

Prevention and treatment of concomitant infections and diseases

A separate application for the prevention and treatment of non-communicable diseases **has not been developed,** which is an area for further work.

Health service delivery

Out of 9 types of measures of a comprehensive package of services on prevention, treatment, and care for PWID, the CP includes 7 related to healthcare services but CP does not mention harm reduction programs for PWID, in particular, needle and syringe exchange, and targeted information and educational activities to promote behavior change.

The Program of the Government of the Kyrgyz Republic on Overcoming HIV Infection in the Kyrgyz Republic for 2017-2021" includes strategies for the decentralization of services, redistribution, delegation, and integration of services but these recommendations are not included in CP.

North Macedonia

According to information from country experts, North Macedonia has no comprehensive national HIV treatment guidelines. The main document regulating a number of aspects of HIV treatment is called the Guidelines for Medical Care in Case of HIV Infection (Упатство за медицинското згрижување при ХИВ инфекција) and dates of 2015 (Ministerial Decree No. 17-2490/1). This document is part of a series of documents adopted under the Law on Health Protection (the main legislative act in the field of the country's healthcare). The revision rules are not stated in the document, however, the text indicated that the next revision should be published in 2016 (however, this did not happen).

On the one hand, the document is mandatory (according to the Law on Health Protection). On the other hand, it is not followed in practice (based on interviews with clinical specialists) mainly because its recommendations are outdated.

There is another document that relates to the treatment of HIV infection, namely the Protocol on the Management of HIV-positive Patients in the General Infectious Outpatient Clinic. It dates as of 2012.

The University Hospital for Infectious Diseases (the only institution providing HIV services) is guided by the latest published guidelines of WHO and EACS.

An important document that regulates the availability of medicines is the Essential Medicines List (Листа на есенцијални лекови). If a particular drug is included in this List, it means that the drug can be purchased even if it is not registered in the country. The prices for drugs included in the List, unlike other drugs, are regulated in accordance with the Law on Medicines and Medical Devices, which contributes to their further reduction.

According to the information received from the expert, the latest revision refers to 2015 (February 9). The List does not contain such clinically significant HIV treatment options as DTG, RAL, DRV, ATV, as well as FDC, including ABC/3TC, DTG/3TC/TDF, EFV/FTC/TDF, EFV/3TC/TDF, FTC/TDF, and 3TC/ZDV. Experts recommend updating the Essential Medicines List in line with the WHO Model List. This measure will allow eliminating uncertainty in terms of the clinical use of a number of drugs and, possibly, will contribute to solving problems with the registration of specific drugs.

In practice, HIV treatment regimens are prescribed in accordance with the latest published WHO's and EACS's guidelines, however, adjusted for the availability of drugs in the Republic of North Macedonia, as well as for cost. In particular, the WHO guidelines, which offer therapy to all HIV-positive people, regardless of the state of the immune system, are observed in practice but is not mentioned in the clinical protocol.

Key Points

Diagnostics

According to the information received from the country expert, the current version of the protocols **is now discussed to simplify the testing algorithm in accordance with the latest WHO guidelines, in particular, refusing the Western Blot test.**

Community-based testing in the country has been conducted in practice since 2007. Currently, 14 NGOs carry out such tests, focusing on vulnerable groups.

ARV drugs for HIV prevention

The current guidelines **only contain general references to PrEP**. A working group has now been established to develop national guidelines for PrEP with the support of a WHO representative.

The protocols contain a PEP section, **which is generally in line with the 2016 WHO Guidelines but has not been updated in accordance with the 2018 recommendations regarding regimen choice.** A working group has now been established to develop new national guidelines on PEP.

Antiretroviral therapy regimens

According to experts, the main first-line regiment is TDF + FTC + EFV.

The national guidelines have **no specific sections on switching to the second- and third-line regimens.**

In clinical practice, whenever possible, preference is given to combination drugs in accordance with WHO guidelines.

DTG is available for a limited number of patients. An expert indicated the patent on DTG and the cost of the original drug as a barrier to expanding access to this drug, recommended by WHO as the first-line therapy. **EFV 400 mg was not available in North Macedonia at the time of writing.** One of the recommendations is to switch regimens from EFV 600 mg to EFV 400 mg as recommended by the 2018 and 2019 WHO Guidelines.

Prevention and treatment of concomitant infections and diseases

In practice, the treatment of comorbidities in the country **is guided by the EACS protocols.** Appropriate sections should be added to HIV treatment protocols.

Health service delivery

National guidelines **do not contain** sections on health care delivery. Relevant sections should be added to the revised document.

In general, the **key recommendation** regarding clinical guidelines in Macedonia is to update the national HIV treatment protocols (or adopt a new document), either taking into account the EACS requirements or taking into account the WHO standards, as well as bringing other regulatory documents governing the provision of medicines, in accordance with international standards. Measures are also recommended to reduce the price of a range of ART (including DTG) to increase access.

Moldova

Within measures to treat HIV infection in Moldova, there are six separate normative acts (the National Guidelines for Laboratory Diagnostics of HIV Infection and 5 National Clinical Protocols) to manage the HIV diagnosis and treatment in adults and adolescents, children under 10 years old, as well as the prevention of mother-to-child transmission of HIV, post- and pre-exposure prophylaxis of HIV infection. All 6 normative acts were approved by the corresponding orders in 2018 (the titles of documents and references to them - see Annex 1).

National Clinical Protocols (NCPs) include mandatory and recommendatory requirements for implementation. The frequency of NCP revision is defined in the protocol itself - usually every 2-4 years, but the protocols can be revised more often, if necessary.

According to the respondents, patient organizations are involved in the revision of national guidelines (in particular, this practice took place in 2017). Patient organizations also take part in the revision of the National Program on Prevention and Control of HIV/AIDS and STIs.

Key Points

Diagnostics

The main method of HIV screening in adults and children over 18 months born to HIV-positive mothers, both in healthcare facilities and at NGOs, **is testing using only rapid tests based on capillary blood, followed by a confirmatory test.**

ARV drugs for HIV prevention

The recommendations on PrEP **are fully consistent with the 2016 WHO Guidelines but they need to be updated in accordance with the 2019 WHO Guidelines,** in particular, the possibility of using short courses of PrEP (on demand), as well as the use of TDF + 3TC.

The recommendations on PEP are almost entirely in line with the 2016 WHO Guidelines but the 2019 WHO Guidelines require changes to be made to recommend DTG, instead of LPV/r, as the preferred third drug for PEP in adults, adolescents and children of appropriate age.

Antiretroviral therapy regimens

First-line ART is slightly different from the regimens recommended by WHO in 2016. The main first-line treatment regimen in adults, adolescents, and children over 6 years is the recommended DTG-based treatment regimens, which subsequently was mentioned in the WHO Guidelines in July 2019. An EFV 600 mg regimen is recommended for women of reproductive age and patients receiving rifampicin-based TB treatment. The NCP on ART for adults and adolescents **completely excluded and did not recommend** the use of d4T- and NVP-based ART regimens, both for children and adults.

The NCP's section "HIV infection in children 0-10 years old" also **completely excludes** treatment regimens based on EFV 600 mg.

The NCP does not provide any recommendations on the use of EFV400 due to the fact that at that time there were no FDC preparations based on EFV400, and its introduction into the NCP would require its purchase for a small number of patients, which would significantly complicate the procurement and prescribing management.

The recommendations for second-line ART in adults and adolescents in the NPC should be changed in accordance with the 2019 WHO Guidelines, and DTG should be used as the main second-line drug in case of NNRTI failure, and in case of DTG failure, boosted PIs ATV/r or LPV/r should be recommended in combination with two other NRTIs.

The recommendations for second-line ART in children younger than 10 years in the NCP are in line with the 2016 WHO Guidelines but unlike them, RAL is recommended as an alternative drug for children who cannot yet use DTG, which is subsequently mentioned in new WHO guidelines as of July 2019.

Prevention and treatment of concomitant infections and diseases

The recommendations on the prevention and treatment of co-infections (HBV, HCV, TB) are well described in the relevant NCPs regarding these diseases, including the specifics of treating these infections affected by HIV infection and taking ART.

The NCP on HIV has neither a brief description nor references to relevant documents. There are also **no recommendations** on the prevention and treatment of the relevant non-communicable diseases.

Health service delivery

The NCP on HIV does not mention issues of decentralization and integration of services. These sections can be included in a revised document or the national program and other normative acts.

Russia

At the time of writing, the clinical aspects of HIV treatment in Russia are regulated by a document titled “Clinical guidelines ‘HIV infection in adults’”. The year of the last revision is 2017, although, at the time of the final report writing, **information about the appearance of a new version of the document as of 2019 became openly available.** According to the latest information, the document has the status of a project. In accordance with the rules, the frequency of revision of clinical guidelines is two years .

The authors of the guidelines are the National Association of Specialists in the Prevention, Diagnostics, and Treatment of HIV Infection. The clinical guidelines are not mandatory, however, according to the Federal Law of December 25, 2018, N 489-FZ “On Amendments to Article 40 of the Federal Law ‘On Compulsory Health Insurance in the Russian Federation’” and the Federal Law ‘On the Basics of Health Protection of the Citizens in the Russian Federation’ on clinical recommendations”, health care is provided based on clinical guidelines.

General remarks

It is important that the medical community and patient organizations take an active part in the discussion of the CP-related project, taking into account the necessary adjustments. It is recommended to provide for the formal participation of representatives from patient organizations in the editorial board of protocols.

It is also worth noting that clinical protocols for children and pregnant women in RF are published separately. Perhaps combining all the recommendations in a single document will make the work more convenient.

Key Points

Diagnostics

Key proposals for revising the current version of the 2017 recommendations:

- It is required to update the data on sufficient timing of antibody testing after a risky situation - prescribe the period of the “serological window”;
- Add information on pre- and post-test counseling;

ARV drugs for HIV prevention

Key proposals for revising the current version of the 2017 recommendations:

- Create clinical guidelines for pre-exposure and post-exposure prophylaxis of HIV transmission, taking into account new data and new treatment regimens.

Antiretroviral therapy regimens

Key proposals for revising the current version of the 2017 recommendations:

- There is a need for a clearer formulation of the treatment initiation for all people with HIV, which excludes the possibility of delaying ART initiation. There are now too many priority categories selected and this creates the illusion that not everyone needs drugs;
- Adjusting first-line regimens: converting DTG to preferred first-line regimens, introducing EFV in a dose of 400 mg;
- Discussion option: conduct a resistance test in all patients before starting therapy in regions with a prevalence of NNRTI resistance above 10%;
- Criteria for therapy failure in the RF recommendations are more stringent in comparison with the WHO guidelines but they comply with the EACS and US DHHS criteria and can be applied in RF if test systems with a sensitivity threshold of fewer than 50 copies/ml are available and if a faster re-examination affected by controlled adherence (2-4 weeks after the first test) is possible. The need for adjustment should be discussed additionally. Experts have expressed concerns that the WHO’s criteria for the therapy failure are too broad;
- Expand the section on assessment and strategies of increasing adherence to treatment.

Prevention and treatment of concomitant infections and diseases

Key proposals for revision of the current version of the 2017 recommendations:

- Mandatory inclusion of a full-fledged section on cardiovascular diseases, the state of the nervous system and mental health, GIT damage
- Necessary introduction of a section on working with people who use drugs, people with mental illness - ensuring adherence and constant support without delaying the start of treatment.

Health service delivery

Key proposals for revision of the current version of the 2017 recommendations:

- It is important to prepare a normative and legal framework with recommendations for decentralization of services; this model is relatively successfully applied in the territories (however, it needs additional training of regional specialists and funding), recommendations for the redistribution and delegation of services (an increase in the number of non-medical personnel or cooperation with NPOs is required)
- The recommendations do not describe the integration of services in connection with HIV infection and comorbidities, although the procedure for treating tuberculosis and HIV is prescribed, which requires interaction with the TB service. It is necessary to prescribe the interaction with the narcological service.

On December 26, 2019, the draft new clinical guidelines of the Ministry of Health of the Russian Federation "HIV-infection in Adults", developed by the National Association of Specialists in the Prevention, Diagnostics, and Treatment of HIV Infection, were published. According to the information received, the approval of these guidelines is expected in the first half of 2020.

The document has additional clarifications to the recommendation to conduct ART for all HIV-infected patients: "Initiation of ART should be recommended regardless of CD4 count and viral load since the use of ART decreases systemic inflammation and reduces the risk of disease."

Other notable changes

- There was an important clarification about the immediate prescription of ART during pregnancy: "It is recommended to consider laboratory confirmation of HIV infection in pregnant women as the criterion for starting ART. Having laboratory confirmation of HIV infection, it is not recommended to postpone the ART initiation until all clarifying test results are received, especially if the infection is detected in the late preterm period (bearing a child). "
- The recommendation to postpone the initiation of ART in the presence of mental illness and severe drug addiction were removed.
- Criteria for monitoring bone health and side effects of treatment were added.

- For the first time, the criteria for conducting a resistance test before starting treatment were mentioned: “Before initiating ART, it is recommended to test for genotypic resistance, preferably immediately after HIV diagnosis; or before initiating ART for all patients in regions with a resistance prevalence more than 10%; in the presence of a high risk of primary resistance to NNRTIs due to the widespread use of this group.”
- The list of drugs that are not recommended for use under certain conditions has been updated. Thus, DTG is not recommended for women in the 1st trimester of pregnancy (teratogenic effect - development disability of the embryo or fetus - is possible).
- For the first time, the recommendation on uninterrupted drug supply was included: “To ensure uninterrupted drug supply at the regional level, one should consider the planning of financial resources to provide the region's expenditure obligations in terms of drug supply for socially significant diseases, including by introducing an additional type of expenditure into the calculation of a visit cost on the “infectious diseases” profile at the AIDS Center. For regions with a high prevalence of HIV infection in the population, it is recommended to use FDC drugs to increase patient adherence to treatment.”
- New sections on pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) were added to the Clinical Guidelines. The sections describe the mechanisms for managing and prescribing PrEP and PEP and the drugs recommended for this.
- The following sections were also added: rehabilitation of patients, prevention of HIV infection, assisted reproductive technologies and artificial insemination affected by HIV infection, pathological diagnostics, as well as a section devoted to the formation of the patient’s adherence to treatment.

Choice of ART regimens

- When choosing first-line ART, use less toxic and more convenient FDC drugs.
- DTG is specified as the preferred option for first-line ART, in line with global ART trends.
- Now, the preferred first-line ART regimen for adults is DTG + 3TC (or FTC) + TDF. Note that there was EFV 600 mg instead of DTG earlier in this regimen.
- Only two regimen options are specified as alternate first-line regimens: DTG + 3TC + ABC and EFV 400 mg + 3TC + TDF.
- It is indicated that EFV 400 mg can be prescribed once a day due to its better tolerability compared to EFV 600 mg, less risk of the treatment discontinuation due to side effects. Previously, EFV 400 mg was mentioned only as a possible treatment option for adults.
- EFV 600 mg is only recommended for special case regimens.

- An important note on EFV was added: “It is not recommended to prescribe EFV 400 mg or EFV 600 mg in regions with a high prevalence of primary drug resistance to NNRTIs. When starting ART with an EFV-containing regimen, it is recommended to perform a resistance test in all patients in regions with a high level of resistance (more than 10%).”
- NVP was excluded from recommended first-line drugs and is now only available as a second-line drug.
- It is said for the first time that it is not recommended to use didanosine due to its high toxicity. The use of the ABC/3TC/ZDV combination is also not recommended due to its low efficacy and the risk of developing resistance.
- DTG + 3TC was added to the list of simplified regimens that can be used.
- Among ARV drugs for special cases, which are recommended for use when it is impossible to use preferred and alternative regimens, it is firstly indicated such modern drugs as DOR, as well as combination drugs elvitegravir/cobicistat/FTC/TAF, DOR/3TC/TDF.

Romania

According to information obtained from the country expert, Romania has not updated national HIV treatment protocols since 2013-2014. National HIV experts, supported by the Ministry of Health, have decided that the protocols of the European AIDS Clinical Society (EACS) may be applied in the country. **The 2016 version of the EACS Guidelines (Version 8.1) was translated into Romanian and suggested as the basis for adaptation; however, new national protocols have not been adopted officially. For the time being, Romania uses the current EACS protocols as a guideline for treating HIV infection.** Among the barriers to accessing the treatment, the expert mentions that not all of the drugs indicated in that document are available for use in Romania. **In particular, single-tablet regimens based on RPV and BIC are not available.**

Key Points

Diagnostics

Two ELISA tests with two different blood samples are used to diagnose HIV infection in Romania, as well as a test for viral load in the blood plasma. Western blot is optional.

ARV drugs for HIV prevention

PrEP costs are not reimbursed by the national HIV program.

The basic PEP regimen is TDF+FTC or AZT+3TC (alternative) + RAL, LPV/r or DRV/r. DTG can be used in case of special circumstances. **DTG is not the drug of choice for PEP due to its cost (DTG generics are not available in Romania due to patent).**

Antiretroviral therapy regimens

Integrase inhibitors (DTG or RAL) are the preferred first-line treatment option. Single-tablet FDCs (ABC + 3TC + DTG) or (TAF + FTC + ELV/COBI) are used to improve adherence.

Boosted protease inhibitors, mainly DRV and ATV, are recommended **as second-line therapy.**

For reasons of savings, DTG is not used for post-exposure prophylaxis (no affordable generic for procurement is available).

EFV 600 mg can be used as an alternative treatment option (in practice, this rarely occurs due to side effects). **EFV400 mg is not recommended for use in Romania.**

EFV and DTG are usually not recommended to be used in pregnant women. Raltegravir is the preferred option.

Pediatric forms of RAL and DTG **are not available** in Romania.

ZDV + 3TC can be used as an alternative option, but this occurs extremely rare in practice (due to the toxicity of ZDV).

Prevention and treatment of concomitant infections and diseases

EACS guidelines are used.

Health service delivery

The expert did not mention any clinically important aspects related to the organization of the service delivery system in Romania.

Serbia

Serbia currently does not have a national HIV treatment protocol. At the same time, national guidelines are planned to be written in the framework of the Strategy on HIV Infection and AIDS for the Period 2018-2025. Currently, as a result of the consensus reached at the meeting of infectious disease specialists in 2011, **Serbia is applying the latest edition of the European AIDS Clinical Society (EACS) guidelines (in this case, as of 2019).** The above-mentioned strategy contains sections devoted to specific aspects of HIV prevention (including pre-exposure prophylaxis) and treatment. It was prepared, inter alia, taking into account the recommendations of the World Health Organization.

Key Points

Diagnostics

The testing algorithm in the country includes two tests for antibodies to HIV, then Western blot or HIV RNA PCR. There are several rapid testing sites where testing is provided by NGOs in collaboration with national healthcare facilities.

The diagnostic guidance is described in the national strategy published in 2019 and, according to an expert; it is in line with the WHO guidelines on HIV diagnosis and prevention.

ARV drugs for HIV prevention

There are no PrEP programs in healthcare facilities of the country. PrEP drugs are available at pharmacies, **but these drugs are not covered by health insurance.**

Health insurance also does not cover PEP, except for children born to mothers with HIV.

The Strategy on HIV Infection and AIDS for the Period 2018-2025 indicates the need to develop national guidelines on PrEP and PEP.

Antiretroviral therapy regimens

- DTG is used as a separate drug in combination therapy only in the second-line therapy (instructions from the Republic Insurance Fund).
- TDF/FTC/EFV is not available in Serbia as a single-tablet regimen.
- DTG/ABC/3TC can be used as first-line therapy.
- TAF is not available in Serbia as part of any HIV regimens.
- Atazanavir/ritonavir and atazanavir/cobicistat are not available in Serbia.
- There are no formal recommendations regarding the preferences of FDC.
- Despite the lack of any official recommendations in this regard, stavudine is not used in Serbia.
- EFV 400 is not used because the EACS guidelines do not have any recommendations on this.

Prevention and treatment of concomitant infections and diseases

Infectious disease specialists who manage HIV-infected patients (there are 10 of them in Serbia, according to the country expert) cannot prescribe drugs for the treatment of comorbidities (for example, antibiotics), and this fact significantly complicates the management of patients with comorbidities.

Health service delivery

HIV services are provided in a decentralized manner in 4 centers.

Tajikistan

The Guidelines on diagnosis, monitoring and treatment of HIV infection in Tajikistan (newborns, children, adolescents, and adults) was developed and approved in 2019. **The development of the document was based on 2016, 2018, and 2019 WHO Guidelines.** The frequency of the protocols revision is not regulated; before, the document was updated in 2010 and 2015.

Key Points

Diagnostics

HIV testing remains voluntary but in some situations (partners of PLHIV, blood donors, and organ donors) testing is mandatory. To improve coverage, non-health workers can provide testing at the community level using rapid testing.

ARV drugs for HIV prevention

The implementation of PrEP is specified in the normative document **but the new 2019 WHO Guidelines on PrEP regimens regarding the choice of the 2 + 1 + 1 method are not mentioned.**

PEP issues are included in the normative documents. **LPV/r or ATV/r** is included as third drugs. Where possible, it is recommended to use RAL, DRV r or EFV as alternatives.

Antiretroviral therapy regimens

- National criteria for ART initiation meet the WHO criteria. Regardless of the CD4 count, ART is recommended for all people with confirmed HIV infection. First of all, ART is prescribed for children under 5 years old, and people with diagnoses of 3 and 4 clinical stages of HIV infection.
- Recommendations for breastfeeding are in line with the WHO guidelines. To reduce the risk of HIV transmission, milk formula is provided free of charge to all children born to HIV-positive mothers up to the age of deregistration (18 months).
- In accordance with the latest 2018 and 2019 WHO Guidelines, DTG is included in the preferred first-line ART regimens, EFV (dosage of 600 or 400 mg) is included in alternative regimens.
- DTG is included in preferred second-line ART regimens.
- General WHO recommendations on the choice of third-line ART regimens are mentioned in national protocols, but specific drugs are not indicated.
- Combination drugs are preferred.
- The use of EFV400 is reflected in the recommendations.
- Stavudine is not used.

Prevention and treatment of concomitant infections and diseases

The national protocol indicates in sufficient detail the management of coinfections, including viral hepatitis, tuberculosis, cardiovascular diseases, depression, etc.

Health service delivery

Considering the WHO guidelines on an integrated approach to the provision of services for PLHIV, including case management, ART prescribing and monitoring in the country, the MHSPP approved the order on the integration of services at the level of primary health care.

Uzbekistan

Treatment of HIV infection in Uzbekistan is carried out in accordance with the document titled “National clinical protocol ‘Dispensary observation of patients with HIV infection’” as of 2018. The legal status of the document is mandatory. The frequency of revision of the national protocol is not regulated by any documents in the country. The editorial board of the current document included leading experts in infectious diseases/HIV infection; representatives of civil society and patient organizations were not included in the panel.

Key Points

Diagnostics

The 2016 WHO Guidelines on retesting all HIV-infected people before starting ART to confirm the correct diagnosis of HIV **is not included in national programs,** since the country is still implementing a three-step confirmation strategy for HIV diagnosis (the 2010 WHO Guidelines).

According to the 2016 WHO Guidelines, in addition to standard HIV-testing services, 140 trust counseling rooms also conduct rapid **testing for key populations,** including needle and syringe programs and condoms distribution there.

ARV drugs for HIV prevention

The recommendations for PrEP and PEP **are fully consistent with the 2016 WHO Guidelines.** TDF/3TC or TDF/FTC is used for PrEP; TDF + 3TC + LPV/r or AZT + 3TC + LPV/r (ATV/r), for PEP.

Antiretroviral therapy regimens

- The criteria for starting ART do not comply with the 2016 WHO Guidelines (ART is recommended to start if the CD4 count is ≤500 cells/mm^3 or if the VL is 100,000 copies or more, regardless of clinical and immunological considerations).
- Since 2018, the country has been purchasing DTG and using it in an alternative first-line therapy, and since 2019, NVP and LPV have been replacing by DTG in the first-line therapy, which is in line with the 2019 WHO Guidelines.
- The FDC drug use takes into account the WHO guidelines.
- Treatment regimens lack the 2016 and 2019 WHO Guidelines on the use of RAL in children and EFV400 in the adult population of PLHIV.
- Pregnancy testing for women of fertile age taking DTG is not performed because these recommendations are not included in the national protocol, and this situation, in turn, creates problems with justifying funding for their purchase.
- Pre-exposure prophylaxis is mentioned in the protocol for HIV-negative partners of serodiscordant couples to reduce the likelihood of the virus transmission to uninfected partners (TDF/3TC or TDF/FTC) and to protect the uninfected partner of serodiscordant couples at the time of impregnation.
- In case of treatment of HIV-infected infants who begin treatment in the first months of life, the national protocol does not contain a step-by-step scenario of ART regimens, more precisely, the scenario for newborns is generalized with the scenario for children under 3 years.
- The national protocol also does not have recommendations to use TDF in children under 10 years old and DTG, in children over 10 years old, due to the high cost of pediatric doses of the above drugs.
- Stavudine and didanosine are not used.

Prevention and treatment of concomitant infections and diseases

The national guidelines have sections on the management of comorbidities that **are generally in line with the 2016 WHO Guidelines.** However, a number of noted discrepancies are listed in the country profile.

Health service delivery

ART for HIV/TB co-infected patients is initiated only at AIDS-service facilities. **The national protocol does not include the WHO guidelines on the prescription of ART to patients of tuberculosis hospitals,** which leads to low and late coverage of ART in patients with HIV/TB, which may contribute to an increase in the number of deaths.

Medical personnel with no special education are not allowed to prescribe ARVs to patients, which contributes to the low coverage of PLHIV with specific treatment at the district level. Patients receive ARVs in AIDS centers or in district medical associations, not far from their place of residence, i.e., the drug supply system has been decentralized for the convenience of patients. This saves the patient's travel expenses and eliminates one of the barriers to adherence to therapy.

According to the 2016 WHO Guidelines, ART should be started and conducted in PWID with HIV where opioid substitution therapy (OST) is provided. **The OST program is not approved by decision-makers, which does not allow this recommendation to be included in the national protocol.**

Despite the achievements in the prevention of perinatal transmission of HIV infection, the issues of family planning among PLHIV and access to modern contraception remain relevant. These 2016 WHO Guidelines should be indicated in the section on provider-initiated HIV testing.

Montenegro

An interview was conducted with a country expert. According to the information received, there are no national protocols for HIV treatment in the country, and at the time of the interview, there was no discussion on the development of such protocols. **According to the decision made by the National Coordination Body for Communicable Diseases of Montenegro, the treatment of patients with HIV infection is guided by the 2017/2018 EACS Guidelines (version 9) adjusted for the availability of drugs in the country and other country peculiarities.**

The expert noted that it is vital to have country treatment protocols, therefore, important further steps will be either renewal of discussions on the implementation of national protocols, or formalizing the EACS Guidelines as the main standard for treating patients with HIV infection in the country.

Key findings and recommendations

This section contains key findings and recommendations based on the study. They are of a collective and descriptive nature, and their main purpose is to reflect some general trends, to varying degrees, usual for the countries included in the project.

Recommendation 1.

Based on the conducted analyzes, initiate discussions to optimize/adopt recommendations for HIV treatment at the national level within the community of specialists with the involvement of experts from WHO, UNAIDS, other UN agencies specialized in clinical aspects of the epidemic response, the European AIDS Clinical Society, non-profit patient organizations.

The authors of the report hope that certain country analyzes will serve as a basis for further discussions to revise/adopt the protocols in the professional community at the national level. This discussion will require further careful analysis to develop optimal solutions to optimize the standards for providing care for people with HIV infection, taking into account the latest scientific evidence and national context. Ideally, such discussions should be held with experts from WHO, UNAIDS, other UN agencies involved in the clinical aspects of the epidemic response, the European AIDS Clinical Society, representatives of non-profit organizations. They can take place in the form of separate meetings or in the framework of already planned thematic conferences.

Recommendation 2.

Provide a prompt mechanism for revision national recommendations on HIV treatment, at least once a year, and, if necessary, as new scientific data become available.

National protocols on the treatment of HIV infection in one form or another are available in almost all analyzed countries, with the exception of Romania and Serbia, where the EACS Guidelines are applied. Moreover, in the framework of the National Strategy 2018-2025, the development of country recommendations is planned in Serbia, and in this regard, it is recommended to take into account the findings of the country analysis (see Annex 2) while working on this document.

The questionnaire included a paragraph on the legally binding or advisory status of national recommendations. Several years ago, when the community of people with HIV in Russia actively advocated the adoption of recommendations for treating HIV infection, one of the additional requirements was to make them mandatory . The analysis showed that clinical guidelines on HIV infection are formally binding in several countries, including Kyrgyzstan, Moldova, Tajikistan, and Uzbekistan. In North Macedonia, the protocols are also formally binding, since they have a legal effect because of the order of the ministry, but in practice, they are not respected due to the fact that the information in them is outdated (the document is dated 2015). In the regulatory and legal framework of several countries, including Russia and Kazakhstan, there are references to guidelines in various normative legal acts regulating the provision of health care. Moreover, in Russia, in addition to recommendations, there are also standards for the HIV treatment, which are approved by the order of the Ministry of Health of the Russian Federation. In Bosnia and Herzegovina, the protocols are advisory, while in Romania and Serbia, in the absence of national recommendations, the ECAS protocols, which are also not legally binding, are used. None of the experts involved noted that the current legal status of the document (mandatory/optional) was a barrier to access services. Due to the fragmented data, it is difficult to make an unambiguous recommendation on whether national treatment guidelines should be binding. This issue is recommended to be addressed in the framework of the discussions mentioned in Recommendation 1.

In some cases, a relatively long time frame can be noted for revising protocols: from three to four years in Bosnia and Herzegovina; from two to four years in Moldova; the frequency of revisions is not regulated in Uzbekistan; in North Macedonia, the protocols have not been revised since 2015, etc. As a general recommendation, an annual revision of the protocols can be proposed and it can be foreseen the ability to quickly make adjustments as new data emerges, as it is used, for example, in guidelines of the American Association for the Study of Liver Diseases (AASLD) or HIV-related guidelines of the US Department of Health and Human Services.

Recommendation 3.

Provide a mechanism for the meaningful involvement of specialized patient organizations in developing national recommendations for the treatment of HIV infection.

Representatives of non-governmental organizations are usually included in the editorial board that develops treatment protocols for the World Health Organization. Among the countries involved in the study, a similar practice exists in Bosnia and Herzegovina and Kyrgyzstan, and public organizations as authors of recommendations are allowed to be included in Moldova. In Kazakhstan, before approval, recommendations are published on a special portal, where any person can comment on them. The same practice exists in Russia with regard to HIV treatment standards. Moreover, there is the experience in publishing draft national recommendations for feedback. The authors of the report recommend all countries included in the study providing for a mechanism for the meaningful involvement of relevant patient organizations in the process of developing national recommendations for HIV treatment.

Recommendation 4.

In the next revisions of national protocols in countries where this is necessary, emphasize the recommendations to offer ARV therapy to all people with HIV infection regardless of the immune status.

One of the key 2016 WHO Guidelines was to offer antiretroviral therapy to all people living with HIV regardless of immune status (CD4 cell count). The national guidelines of almost all analyzed countries, in one way or another, have the WHO “test and treat” strategy, namely, the text includes recommendations to offer antiretroviral therapy to a person regardless of the CD4 cell count. The exceptions are Uzbekistan, where a step-by-step transition to the “test and treat” strategy is planned due to financial constraints and insufficient readiness of the health care system, and North Macedonia, where this strategy is being implemented in practice but is not mentioned in the outdated version of the protocols as of 2015. In any case, the next revisions of national protocols, where necessary, should emphasize the recommendations to offer ARV therapy to all people with HIV infection regardless of their immune status.

Recommendation 5.

When discussing new revisions of national protocols, revised WHO guidelines regarding the use of DTG as the preferred first-line treatment option and EFV400 as an alternative first-line treatment option should be taken into account.

The national recommendations of most of the countries included in the study do not reflect the 2019 WHO Guidelines regarding the inclusion of DTG in preferred first-line regimens (with the exception of Moldova and Tajikistan) and the inclusion of EFV at a reduced dosage of 400 mg in alternative regimens (with the exception of Kazakhstan, Kyrgyzstan, Tajikistan, draft revised recommendations in the Russian Federation). In some countries (particularly, in North Macedonia), it is indicated that the use of DTG in clinical practice is limited because of its high cost.

Countries of the region should include in national clinical protocols the scenarios of switching to DTG for those who already use other regimens (including women of fertile age) to respond when the availability of DTG in the country improves (the 2019 WHO Guidelines contains main switching scenarios).

Regarding EFV 400 mg, countries should develop a separate strategy, taking into account marketing and price barriers, the need for further use of EFV in general and replacement of EFV 600 mg with EFV 400 mg in some countries.

Recommendation 6.

Consider the inclusion in national treatment protocols of integrase inhibitors with a high barrier to resistance, which could potentially become an alternative to DTG in case of its low availability.

Due to problems with the availability of dolutegravir, noted by experts, for example, in Belarus and North Macedonia, it is necessary to consider the inclusion in national protocols of integrase inhibitors with a high genetic barrier of resistance, which could potentially become an alternative to less available DTG: for example, BIC is at least for population groups, the effectiveness and safety of the drug with sufficient evidence (non-pregnant adults, without a high risk of tuberculosis coinfection).

Recommendation 7.

Pay special attention to the use of fixed-dose combinations (FDC) in new editions of national protocols

With regard to the use of combined forms in the countries included in the study, no uniform approach was found. National guidelines of some countries do not reflect the preference for FDC (for example, Macedonia and Kyrgyzstan), but they are used in clinical practice. In other countries (for example, Belarus and the Russian Federation), the recommendations specify that preference should be given to FDC, but the situation in clinical practice is different (which may be related rather to accessibility and organization of the procurement process, than to clinical aspects). In any case, countries should pay special attention to the use of FCD in the next edition of the protocols.

Recommendation 8.

A new version of the protocols should take into account the revised 2019 WHO Guidelines on the testing algorithm, as well as a paragraph on the participation of NGOs in HIV testing.

The main aspects in diagnostic to consider when revising current HIV treatment guidelines are the revised WHO Guidelines on testing algorithms , as well as recommendations regarding the involvement of non-governmental organizations in the testing process: “lay providers who have undergone special training, under the supervision of specialists, can conduct safe and effective HIV testing on their own using rapid tests”. Barriers to widespread involvement in ART in a number of countries can be the duration of the testing algorithm (use of IB as a confirmatory test, limited use of RT) and the duration of the chain from test performing to treatment delivery (logistics of the client/patient pathway from the primary testing point to the point of treatment delivery).

Recommendation 9.

Where necessary, national protocols should include sections on PrEP and PEP in line with the latest WHO Guidelines, including the logistics of providing ARVs for PrEP and PEP.

The experts noted that clinical guidelines for the HIV treatment in some countries lacked sections on pre-exposure prophylaxis (e.g., Belarus, Kazakhstan, and North Macedonia), and in some cases, post-exposure prophylaxis (Belarus). Among other things, it was suggested that the availability of ARV drugs for PrEP and PEP may be a problem: a doctor provides them only according to certain narrow indications, or it is possible to buy them independently in a drug store or receive them through NGOs. Where necessary, national protocols should include sections on PrEP and PEP in line with the latest WHO Guidelines, describing the logistics of providing ARVs for PrEP and PEP.

Recommendation 10.

Where necessary, based on the results of the country analysis, supplement the clinical guidelines with sections on comorbidities and the use of ARVs for HIV prevention, and update the information in the guidelines, if necessary.

In a number of cases, experts noted that the national recommendations do not have sections on comorbidities (for example, in Kyrgyzstan, there is no section on the treatment of non-communicable diseases) and the use of ARV drugs for the HIV prevention (for example, in Belarus). Countries should be encouraged to analyze the availability and content of national recommendations on issues that are often not included in the current editions of protocols but are relevant to the health of PLHIV in the world (mental health, problems associated with the aging of the population) and specifically in the EECA region (tuberculosis with multi-drug resistance). In countries, where this is not available, it is necessary to consider the possibility to include tables (or links to websites) on drug interactions between ARVs in the protocol texts; this is relevant for health workers, and similar tables are available, for example, in the EACS Guidelines.

Recommendation 11.

Where necessary, based on the results of the country analysis, supplement the sections on the management of vulnerable groups of patients (including PWID) with recommendations focusing on ensuring adherence, support, and immediate treatment initiation.

In most countries, clinical guidelines contain sections on the management of vulnerable patient groups, including people who use drugs. In the clinical guidelines of the Russian Federation and Uzbekistan, this section should be expanded with a focus on ensuring adherence, support, and immediate initiation of treatment. The national analyzes of Kyrgyzstan and the Republic of Belarus also indicate the need to expand the section on working with PWID.

Recommendation 12.

Where applicable, it is necessary to supplement the clinical guidelines with sections on health services delivery (in particular, decentralization of services, the interaction of separate health services, NPOs) or expand the existing sections based on the latest WHO Guidelines and taking into account the specifics of the national health system

The national recommendations of a number of countries (including Uzbekistan, Kazakhstan, and Belarus) do not contain detailed sections on the provision of health services. Where applicable, clinical guidelines should be supplemented with relevant information or existing sections should be expanded based on the latest WHO Guidelines, taking into account the specifics of the national health system.

Recommendation 13.

Hold consultations with WHO experts to develop optimal criteria for determining the threshold for the effectiveness of ART.

It should be noted that during the work, several experts suggested that the current WHO criteria for determining the therapy effectiveness (less than 1,000 copies) are too broad. It was noted that it was necessary to discuss with WHO experts the feasibility of applying more stringent criteria.

Recommendation 14.

When the country context changes regarding the availability of CD4 tests, conduct consultations with participants of WHO experts to stop CD4 cell count monitoring.

According to the analysis, the majority of countries (for example, Belarus, Russia, Bosnia and Herzegovina, Serbia, and Romania) do not follow the WHO Guidelines related to stop monitoring of CD4 cell count when the patient's condition is stable while taking antiretroviral therapy and viral load is constantly undetectable, as well as recommendations on clinical monitoring and CD4 monitoring as a criterion for the ART effectiveness when viral load monitoring is not possible.

Recommendation 15. Conduct negotiations with WHO to concretize the recommendations on the use of dolutegravir in pregnant women, taking into account the new data and their implementation at the protocol level and in clinical practice.

During interviews with experts, it was discovered that there is still no unified position on the prescription of dolutegravir in pregnant women, as new data emerge. It is recommended to consult with WHO on this issue to further concretize the recommendations and implement them at the level of national protocols and in clinical practice.

Annex 1.

List of national clinical guidelines for HIV treatment in EECA and SEE countries

Belarus

- Clinical protocol “Diagnosis and treatment of patients with HIV infection”, 2017
- Clinical protocol “Prevention of mother-to-child transmission of HIV”, 2018

Bosnia and Herzegovina

- Clinical Guidelines for HIV and AIDS Treatment, Sarajevo, 2016.
- HIV Counseling and Testing, Sarajevo, 2016.

Georgia

- Consolidated guidelines on the use of antiretroviral drugs for the prevention and treatment of HIV/AIDS (in Georgian)
- National strategic plan and national HIV program (in Georgian)

Kazakhstan

- Clinical protocol for diagnosis and treatment of HIV infection in adults, 2017

Kyrgyzstan

- Clinical protocols on HIV infection for outpatient and inpatient levels of health care, 2017

North Macedonia

- Guidelines for medical care regarding HIV infection (in Macedonian: “Упатство за медицинското згрижување при ХИВ инфекција”)

Moldova

- National guidelines on laboratory diagnosis of HIV infection, 2018
- National Clinical Protocol No. 211 “HIV infection in adults and adolescents”, 2018
- National Clinical Protocol No. 315 “HIV infection in children 0-10 years old”, 2018
- National Clinical Protocol No. 316 “Prevention of mother-to-fetus transmission of HIV infection”, 2018
- National Clinical Protocol No. 314 “Post-exposure prophylaxis of HIV infection”, 2018
- National Clinical Protocol No. 313 “Pre-exposure prophylaxis of HIV infection”, 2018

Russia

- Clinical guidelines “HIV infection in adults”, 2017
- Project “Clinical guidelines ‘HIV infection in adults’”

ANNEX 1.
LIST OF NATIONAL CLINICAL GUIDELINES FOR HIV TREATMENT IN EECA COUNTRIES

Romania	• EACS Guidelines 2016 (in Romanian)
Serbia	• EACS Guidelines 10.0 (2019, in English)
Tajikistan	• Guidelines on the diagnosis, monitoring and treatment of HIV infection in Tajikistan
Uzbekistan	• On the implementation of national clinical protocols for HIV infection
Montenegro	• EACS Guidelines 2017 and EACS Guidelines 2018

Annex 2. Country Profiles

Belarus

National regulations

Tables 1.1 and 1.2 provide a list of the National Clinical Protocols and the main national regulatory documents that determine the management and procedure for assistance regarding HIV infection and comorbidities. Documents are obligatory for execution: Orders of the MoH of RB - by institutions of the system of the MoH of RB, Resolutions of the MoH of RB and Laws of RB, including institutions that are not part of the MoH system

Table 1.1. National Clinical Protocols

No.	Document name (abbreviation)	Year of the current edition	Document type, number, and date of approval	Access mode
1	Clinical protocol "Diagnosis and treatment of patients with HIV infection" (CP HIV 2017)	2017	Resolution of the Ministry of Health of the Republic of Belarus, dated June 01, 2017, No. 41	http://minzdrav.gov.by/upload/dadvfiles/001077_878477_41_vich.pdf
2	Clinical protocol "Prevention of mother-to-child transmission of HIV infection" (CP PMTCT HIV 2018)	2018	Resolution of the Ministry of Health of the Republic of Belarus, dated June 28, 2018, No. 59	http://pravo.by/document/?guid=3961&p0=W21833281p
3	Clinical guidelines for the treatment of tuberculosis and its drug-resistant forms (CP TB 2017)	2017	Order of the Ministry of Health of the Republic of Belarus, dated May 30, 2017, No. 601	https://www.bsmu.by/downloads/vrachu/instrukcii/2017/601.pdf
4	Clinical protocol "Diagnosis and treatment of patients (adults) with chronic viral hepatitis B and C" (CP VH 2019)	2019	Resolution of the Ministry of Health of the Republic of Belarus, dated March 19, 2019, No. 19	http://pravo.by/upload/docs/op/W21934091p_1557781200.pdf

Table 1.2. Main national regulations governing the management and procedure for assistance regarding HIV infection and related diseases

No.	Document name	Year of the current edition	Document type, number, and date of approval	Access mode
1	On the prevention of the spread of diseases that pose a danger to public health, human immunodeficiency virus	2017	Law of the Republic of Belarus dated January 7, 2012, No. 345-3	http://kodeksy-by.com/download.php?id=2545
2	Subprogram 5 "Prevention of HIV infection" of the State program "Health of the people and demographic security of the Republic of Belarus for 2016 – 2020"	2016	Appendix 5 to the Resolution of the Council of Ministers of the Republic of Belarus, dated March 14, 2016, No. 200	http://minzdrav.gov.by/dadvfiles/000111_759481_postan200.doc (starting from p.185)

3	On the establishment of clinical indications for which persons are subject to compulsory medical examination, and the list of other categories of persons subject to compulsory medical examination	2012	Resolution of the MoH of RB, dated July 12, 2012, No. 97	http://minzdrav.gov.by/upload/lcfiles/000127_164613_PostMZ_N97_2012.doc
4	Instructions on the procedure for management of medical care to persons infected with the human immunodeficiency virus	2017	Resolution of the MoH of RB, dated Nov. 08, 2017 No. 93	http://pravo.by/upload/docs/op/W21732603_1513112400.pdf
5	Instructions on the procedure for management of the consultative and dispensary HIV department	2018	Order of the MoH of RB, dated July 17, 2018, No. 715	http://pmplus.by/press-room/news/715.pdf
6	Instructions on the procedure for organizing the provision of anti-tuberculosis care to patients with HIV infection	2018	Order of the MoH of RB, dated Lune 04, 2018, No. 573	--
7	Regulations on the procedure for monitoring antiretroviral therapy in patients with HIV infection, drug prevention of mother-to-child transmission of HIV, post-exposure prophylaxis of HIV infection	2012	Order of the MoH of RB, dated Nov. 16, 2012, No. 1359	http://goicb.by/wp-content/docs/new/MZRB-Prikaz-2012-11-16-1359.pdf
8	On improving the work of the republican register of patients with HIV infection	2019	Order of the MoH of RB, dated April 17, 2019, No. 459	http://rnpcmt.belcmt.by/files/Site/Registry%20Statement_HIV.pdf
9	The list of diseases that give citizens the right to free provision of medicines dispensed by prescriptions of doctors within the essential medicines list, during outpatient treatment, as well as medical nutrition	2009	Resolution of the Council of Ministers of RB, dated November 30, 2007, No. 1650 (as amended on October 23, 2009, No. 1390).	--
10	Essential Medicines List	2018	Appendix to the Resolution of the MoH of RB, dated August 13, 2018, No. 65. Table 2.	http://minzdrav.gov.by/upload/dadvfiles/!Постановление%20МЗ%20РБ%20от%2013.08.2018%20№%2065.pdf
11	On the establishment of the Republican formulary of medicines for 2018	2018	Resolution of the MoH of RB, dated April 03, 2018, No. 33	http://pravo.by/document/?guid=3961&p0=W21833004

ANNEX 2. COUNTRY PROFILES
BELARUS

Most of the issues considered in the WHO Guidelines are regulated by the CP HIV 2017 or other national regulatory documents (Table 1.3). At the same time, a number of issues included in the WHO Guidelines are not regulated in any way: these are issues of PEP and PrEP, some issues of management of programs and services, procedural issues regarding creation, dissemination, and evaluation of the Guidelines.

Table 1.3. Sections of the WHO Guidelines included and not included in the CP HIV 2017

Issues resolved by the CP HIV 2017	· Diagnosis of HIV infection · ART · Prevention, screening, and management of major OIs · TB screening · Some issues of health service delivery
Issues fully or partially resolved by other regulatory documents	· Prevention and management of TB · Prevention, screening, and management of VH · Prevention, screening, and management of concomitant somatic pathology and mental conditions (partially) · Provision of health services (partly) · Monitoring and evaluation (partially)
Unresolved issues	· ARV drugs for the prevention of HIV infection (PEP, PrEP) · Methods regarding creation, dissemination, and evaluation of the Guidelines

General questions and procedures.

The goal of the CP HIV 2017 is to establish general requirements for the provision of specialized health care to patients with HIV infection. The target audience is defined as employees of the health care system of Belarus; "The requirements [...] are mandatory for legal entities and individual entrepreneurs providing medical activities in the manner prescribed by the legislation of the Republic of Belarus."

It is not separately specified that the protocol is based on specific guidelines, although some of them are mentioned below in the text (for example, universal access to therapy and adherence as the basis for achieving the 90-90-90 target), and that the protocol aims to implement previously defined national tasks (for example, formulated in the profile program of the state). It is not indicated that the provision of medical care, regulated by the protocol, is part of the "continuum of prevention, treatment and other care for HIV infection", and it is not emphasized that "the implementation of the recommendations should be accompanied by efforts to ensure and protect the rights of people in need of services of the system regarding the fight with HIV-infection."

Given definitions are broadly consistent with those used in the WHO Guidelines, with minor differences (for example, "key populations at higher risk" instead of "key populations") and a few oversights (for example, there is no terminology related to PrEP and PEP, point of care testing, participation in assisting by lay workers and the very concepts of "comprehensive services" and "continuum of care for HIV infection").

The CP HIV 2017 does not indicate the authors (developers); it is unclear whether the text of the protocol is the result of their joint discussion or simply each of the authors wrote their own part. The creation of clinical protocols, approved by the MoH, does not provide for involving representatives of public/patient organizations - they are developed and reviewed exclusively by medical professionals.

The CP HIV 2017 does not describe the development procedure, including the regulation of conflicts of interest, the main sources of information used (including no reference to the WHO 2016 Guidelines, which were the main source during the development of the protocol), methods for the synthesis of evidence and a system for assessing the quality of evidence, procedures for resolving controversial issues and an independent peer review (despite the fact that it was probably conducted - all clinical protocols approved by the MoH go through an external peer review system).

The CP HIV 2017 does not define the format for presenting the recommendations, does not indicate the level of evidence and strength of individual recommendations. The option of revising the recommendations has not been laid down, and its regularity (likely timing of revision) and procedure have not been defined.

There is no summary of the recommendations broken down into new and previous ones (not modified, or revised and updated in this protocol), provisions of good practice are not formulated.

Part 2. Diagnostic recommendations

HIV diagnostic algorithms

The CP HIV 2017 contains standard algorithms for laboratory diagnosis of HIV infection in patients aged up to 18 months and over 18 months (Annex 1, Chapters 1 and 2), which take into account the WHO Guidelines to retest all persons with a primary positive HIV test result (Chapter 2.2 of the 2016 WHO Guidelines). So, when testing patients older than 18 months, the following is carried out:

1) Screening examination of the first blood sample by ELISA/ICA or RT for blood, and with a positive result -

2) Arbitration examination, including

- Examination of the second blood sample by ELISA ICA methods using test systems with different antigenic characteristics, and in case of a positive result - a confirmatory examination of the same second blood sample by the IB method (in the case of an undetermined IB result - with a repeated arbitration examination of blood collected after 2-4 weeks),
- Additional determination of HIV RNA concentration (viral load) by PCR method for "patients with signs of illness similar to opportunistic diseases or acute HIV infection".

The procedure for sending blood samples, the order and transfer of information about the results of the examination to health care facilities, and the epidemiological service, as well as the inclusion of data in the State Register of Patients with HIV Infection. Re-testing of those receiving ART is theoretically possible if they conceal their HIV status and only at the stage of screening examination by RT method or through anonymous screening testing by ELISA/ICA method but not in the case of delivery of not anonymous blood sample to the laboratory since the laboratory staff verifies the personal data indicated on the sample with the State Registry of Patients with HIV Infection: the WHO recommendation to avoid retesting of people with established HIV infection is being implemented (Chapter 2.2).

The given survey algorithm is the same for populations with both low (<5%) and high HIV prevalence (> 5%, in Belarus, they are PWID, MSM, and female CSW), despite the fact that the 2016 WHO Guidelines suggest the possibility to shorten the testing algorithm with confirmation of HIV infection based on two positive tests for populations with high HIV prevalence (Chapter 2.7).

According to the CP HIV 2017, rapid testing is possible only with blood RT testing, but not saliva - WHO does not impose such restrictions (the 2016 WHO Guidelines, Chapter 2.7). The indications for the use of RT have been determined, including "voluntary testing for HIV infection of people from population groups with a high risk of HIV infection", but the result of RT is regarded as primary positive only if it is obtained "during a blood test in a healthcare organization" with the obligatory fixation of it "in the patient's medical records"(Chapter 1, item 2), and the second (re-collected) blood sample is sent to the arbitration laboratory by the "healthcare organization"(Chapter 1, item 5.1.2). This contradicts

the WHO recommendation that "lay providers who are trained and supervised can independently conduct safe and effective HIV testing using rapid diagnostic tests" (the 2016 WHO Guidelines, Chapter 2.4.1). The WHO good practice provision also is not implemented "Trained and supervised non-laboratory staff, including laypeople, can undertake blood finger-prick for sample collection." (the 2016 WHO Guidelines, Chapter 6.8). That is, NGOs are legally excluded from the testing process, which is a barrier in the chain from examination to provision of treatment. In reality, NGOs conduct saliva RT but they are not recognized by the healthcare system as a primary HIV test (which makes the testing chain longer), or NGOs hire healthcare workers to collect fingersticks from clients for blood RT (which increases the cost of providing low-threshold care).

Provider-initiated HIV testing

In Belarus is conducted following the 2016 WHO Guidelines (Chapter 2.4.2) "to all who applied [...] with possible symptoms or signs of HIV infection". The CP HIV 2017 does not consider this issue, but the MoH approved lists of clinical indications for HIV testing,[5,6,7,8] mandatory for healthcare facilities of ny profile. Some difficulty is that there are at least four valid lists at the same time, but the differences between them are not so significant. HIV testing is regulated in case of established or suspected tuberculosis[9]. Deviation from the 2016 WHO Guidelines: there are no separate indications for offering voluntary HIV testing to "partners of HIV-infected TB patients" - only "compulsory medical examination" is regulated, which stipulates only the need for an examination "in the presence of epidemiological indications", without their details. The documents do not contain recommendations on the proposal "HIV testing to all children without exception, whose parents are living with HIV" (the provision of good practice in chapter 2.5.4 of the 2016 WHO Guidelines): only the examination of children born to HIV-infected mothers and children breastfed by the time the mother was diagnosed with HIV are defined (CP PMTCT HIV 2018, Chapter 3). There are guidelines for the management of children who "are at high risk of infection due to breastfeeding" (CP PMTCT HIV, Chapter 8). The need for access to RT in healthcare facilities for testing patients with unknown HIV status was determined: pregnant women during childbirth or registration for more than 20 weeks, hospitalized for tuberculosis treatment, with clinical manifestations similar to acute or 3-4 stages of HIV infection, during a voluntary medical examination, as well as in an emergency with biological material (CP HIV 2017, Chapter 1). A recommendation on compulsory testing, not supported by the WHO, is legally fixed[10].

Community-based HIV testing services

Including at low-threshold services of NGOs, as mentioned above, are not provided for by law (the 2016 WHO Guidelines, Chapter 2.4.2).

Regulatory documents of Belarus do not have any list of populations healthcare workers or community service workers should offer voluntary HIV testing.

5 On the establishment of clinical indications for which persons are subject to compulsory medical examination, and the list of other categories of persons subject to compulsory medical examination. Resolution of the MoH of RB, dated July 12, 2012, No. 97. http://minzdrav.gov.by/upload/lcfiles/000127_164613_PostMZ_N97_2012.doc
6 The list of contingents subject to examination for the presence of antibodies to the human immunodeficiency virus. Approved by the Resolution of the Chief Public Health Officer of RB, dated March 27,2003, No. 27.
7 On medical examination for HIV (List of persons subject to medical examination for HIV). Letter of the MoH of RB, dated December 18, 2009, No. 02-2-04 / 4037.
8 The list of contingents subject to examination for the presence of antibodies to the human immunodeficiency virus. Approved by order of the MoH of RB, dated December 16, 1998, No. 351. Appendix 8.
9 On approval of the instruction on the procedure for the provision of anti-tuberculosis care to patients with HIV infection. Order of the MoH of RB, dated June 04, 2018, No. 573.
10 On the prevention of the spread of diseases of the human immunodeficiency virus that pose a danger to public health. Law of RB, dated January 7, 2012 No. 345-3. http://kodeksy-by.com/download.php?id=2545

Only mandatory testing (for certain categories of persons) and compulsory testing (conducted without the consent of the person, but not actually applied) are regulated[11].

Measures to protect personal information (the 2016 WHO Guidelines, Chapter 2.3) are regulated in the framework of the concept of medical confidentiality at the level of the Law "About Health Care" (Article 46). According to the Constitution (Article 22), "everyone is equal before the law and has the right to equal protection of their rights and legitimate interests without any discrimination", although there is no specific anti-discrimination legislation regarding HIV.

Diagnostic algorithms for children under 18 years of age

In accordance with the WHO Guidelines, virological testing is used in Belarus when examining children under 18 months of age, and in addition to testing infants, virological testing of HIV-exposed children at birth has been introduced (the 2016 WHO Guidelines, Chapter 2.5). So, according to the CP HIV 2017, when testing HIV-exposed patients under the age of 18 months, blood is taken for the qualitative determination of HIV DNA by PCR three times: at the age of 2-5 days, 8-10 weeks and 4 months (or, in the presence of clinical signs of immunodeficiency - at any age), with repeated blood sampling and testing in case of a primary positive test result, with confirmation of the diagnosis with two positive tests, or with the transition to subsequent serological testing of a child older than 4 months with three negative results of PCR tests. The timing of subsequent serological testing is not separately regulated (compared to the 2016 WHO Guidelines suggesting that the first serological examination should be conducted at the age of about 9 months); also the possibility of using RT is not mentioned.

ART in Belarus is initiated in infants only with an established diagnosis of HIV infection (in the case of two positive PCR tests in two separate blood samples), and not after the first positive PCR result, as suggested in the 2016 WHO Guidelines (of course, "immediately started ART keeps life" but in Belarus, there is an opportunity to get the result of the second PCR test rather quickly).

When testing non-exposed HIV patients under the age of 18 months according to clinical or epidemiological indications, according to the CP HIV 2017, in the case of a primary positive ELISA/ICA test, repeated blood sampling is conducted for the qualitative determination of HIV DNA by PCR and, if it is negative, the determination is repeated HIV DNA not earlier than one month from the first PCR test.

Minimum thresholds for the sensitivity and specificity of tests for testing infants in serological and PCR studies are not legally defined in Belarus (according to the WHO Guidelines, ≥99% and ≥98% for serological tests and ≥95% (better> 98%) and ≥98% for virological tests, respectively); the maximum allowable time for the issuance of testing results is not determined (according to the WHO Guidelines, no later than four weeks from the moment of sample collection). Belarus does not use WHO-recommended methods for point-of-care testing such as NAT, as the country's pediatric care is well developed to ensure that a blood sample is collected and transported to a laboratory for quality PCR testing.

11 Law "On the prevention of the spread of diseases of the human immunodeficiency virus that pose a danger to public health"

Testing individuals from other priority populations

As for other priority populations (the 2016 WHO Guidelines, Chapter 2.6), the regulatory documents of Belarus govern in detail the testing of pregnant women (the CP PMTCT HIV 2018) but almost do not contain specific recommendations for testing adolescents, couples and partners, as well as certain key populations (the CP HIV 2017 defines them as PWID, MSM, and TG, female CSW, persons in PDLs and migrants).

Under the 2016 WHO Guidelines (Chapter 2.6.2), Belarus provides for HIV testing at the initiative of healthcare provider "for women as a standard component of health care in all antenatal care systems, maternity wards, postnatal wards", as well as in pediatric institutions in cases of suspected HIV infection in a child. HIV testing is included in the package of other tests provided to pregnant women. Testing is conducted using ELISA/ICA or blood RT. Despite the WHO Guidelines on double testing of all pregnant women, in Belarus, testing is conducted once when registering for pregnancy, and only pregnant women at risk are tested again at 28-30 weeks (HBV and/or HCV co-infection, injecting drug use, STIs during the last year) and if the HIV status of their sexual partner is not known; pregnant women are as well tested at any time if there are clinical and/or epidemiological indications specified in the protocol (the CP PMTCT HIV 2018, Chapter 3). If you have an HIV-positive partner who has not had viral suppression for at least the last 6 months, the pregnant woman is examined at registration and then every 4 weeks until delivery. When a pregnant woman who has not previously been tested for HIV is hospitalized for delivery or when a woman in labor who has not previously been tested for HIV is admitted, RT is performed. Despite the prevalence of breastfeeding, Belarus does not follow the WHO Guidelines to retest breastfeeding mothers seronegative for HIV throughout the entire period of breastfeeding, due to the low risk of infection.

Following the 2016 WHO Guidelines (Chapter 2.6.3), counseling on HIV-related issues is provided for partners of pregnant women and they are offered one-time testing after registration of the pregnant woman (the CP PMTCT HIV, 2018). There are no other guidelines for offering voluntary testing for couples and partners. There is a criminal offense for a positive partner in a serodiscordant couple for "putting [negative partner] at risk of infection," which can be a barrier to testing.

HIV testing is not on the list of simple medical interventions[12] adolescents aged 14 and older can consent to (Article 44 of the Law About Health Care"), however, some low-threshold services offer HIV testing for adolescents, for example, Adolescent-Friendly Centers.

In terms of key populations, mandatory screening of "people who use drugs" (upon detection and then annually with a negative result) and "persons in custody" (upon admission) is defined[13]. Some aspects of counseling specific key groups are given in non-binding guidelines for counseling while HIV testing[14].

12 On the establishment of a list of simple medical interventions. Resolution of the MoH of RB, dated May 31, 2011, No. 49. http://minzdrav.gov.by/upload/lcfiles/000127_464830_N49_2011.doc
13 On the establishment of clinical indications for which persons are subject to compulsory medical examination, and the list of other categories of persons subject to compulsory medical examination. Resolution of the MoH of RB, dated July 12, 2012, No. 97. http://minzdrav.gov.by/upload/lcfiles/000127_164613_PostMZ_N97_2012.doc
14 Recommendations for voluntary counseling while HIV testing. N.V. Goloborodko, G.V.Lapitskaya. User's manual. Reg. number 134-1211. Approved. MoH RB Dec.23, 2011 http://pmplus.by/upload/iblock/356/instruktsiya-dkt.pdf

Part 3. ARVs for HIV prevention

At the legislative level in Belarus, only the issues of PMTCT of HIV are regulated (provision of ARV drugs to a pregnant woman, a woman in labor, and a newborn), but the issues of PrEP and PEP for HIV are not regulated (for any population groups). The State Program provides for the procurement of ARV drugs for ART and PMTCT HIV but not for other preventive purposes. The logistics of receipt, storage, and distribution of drugs for PrEP and PEP in healthcare facilities is not specified anywhere; the possibility of providing drugs at community-led point of services is not specified. Nevertheless, "to carry out emergency post-exposure prophylaxis" is indicated in the tasks performed by the CDD regarding HIV infection[15].

Pre-exposure prophylaxis

According to the 2016 WHO Guidelines, "TDF-based oral PrEP should be offered as an additional prevention measure to individuals at significant risk of HIV infection [that is, above 3 per 100 person-years] as part of a combined approach to HIV prevention" (Chapter 3.1) PrEP is not mentioned in any of the regulatory documents of Belarus. In practice, a pilot project on PrEP among MSM was launched in 2019 (the planned coverage is 100 people). Some discordant heterosexual couples, in which a woman is HIV-negative, also use PrEP for the period of impregnation, independently buying ARV-drugs for its use outside Belarus or illegally (ARV-drugs are not sold in the pharmacy network of Belarus, physicians do not issue drugs for PrEP).

Post-exposure prophylaxis

According to the 2016 WHO Guidelines, HIV PEP is prescribed when a high risk of HIV infection is identified; it has been conducted for 28 days, preferably with a three-drug regimen (Chapter 3.2). Several Belarus regulations describe measures to be taken in the event of professional contact of a healthcare professional with patient's body fluids, including a post-exposure testing algorithm[16,17,18], however, they do not contain recommendations on assessing the level of risk of HIV infection (determining the indications for prescribing PEP) and on the use of ARV drugs for HIV PEP (by regimen and duration). PEP after everyday (non-professional) contact is also not regulated by any documents. The guidelines for counseling while HIV testing indicate that the main goal of counseling a patient after unprofessional exposure to HIV is to identify risk factors that led to contact and to look for ways to prevent them in the future, that is, to behave safely[19]. In practice, PEP is conducted in case of professional contacts and domestic non-sexual contacts. In this case, ARV-drugs can be obtained at a healthcare facility.

PEP regimens for PMTCT of HIV in Belarus (the CP PMTCT HIV 2018) depend on when the mother's HIV status is established and whether viral suppression has been achieved within 4 weeks before delivery (Table 3.1).

15 On approval of the Instruction on the procedure for organizing the work of the consultative and dispensary department on HIV infection. Order of the MoH of RB, dated July 17, 2018, No. 715. http://pmplus.by/press-room/news/715.pdf
16 The instruction for the prevention of nosocomial HIV transmission and the prevention of occupational infection of medical workers. Appendix 5 to the Order of the Ministry of Health of the Republic of Belarus, dated December 16, 1998, No. 351.
17 Letter of the Ministry of Health of the Republic of Belarus "On clarification", dated January 13, 2012, No. 10-27 / 17-59, paragraphs 3, 4, 5
18 Sanitary norms and rules "Requirements for the organization and conduct of sanitary and anti-epidemic measures aimed at preventing the emergence and spread of viral hepatitis." Approved by the directive of the Ministry of Health of the Republic of Belarus, dated February 06, 2013, No. 11.
19 Recommendations for voluntary counseling while HIV testing. N.V. Goloborodko, G.V.Lapitskaya. User's manual. Reg. number 134-1211. Approved. MoH RB Dec.23, 2011 http://pmplus.by/upload/iblock/356/instruktsiya-dkt.pdf

Table 3.1. PEP regimens for PMTCT of HIV in the newborn (simplified from the CP PMTCT HIV 2018)

Pregnant	Child	ARV regimen for the newborn*
In ART with viral suppression (VL undetectable at 34-36 weeks)	-	AZT, 2 times a day, for 28 days
In ART without established viral suppression/without ART/primary positive for ELISA/ICA or RT	Full-term	AZT, 2 times a day, for 6 weeks + 3TS, 2 times a day, for 2 weeks + NVP, 3 doses (first 6 hours, 2 and 6 days of life) Discontinue if mother is IB negative
	Premature <34 weeks	AZT, 2 times a day, for 6 weeks

**Notes: initiation of ARV for newborns in the first 6 hours of life, if the mother did not receive ART during childbirth, then in the first 2 hours.*

In Belarus, if the risk of vertical HIV infection is high (pregnant women who received ART for less than 4 weeks or with an undetermined virus suppression for 4 weeks before delivery, or those who did not receive ART, or are primarily positive based on ELISA/ICA or RT), newborns receive tree-component PEP scheme according to US DHHS guidelines[20] and not two-component under the 2016 WHO Guidelines (Chapter 4.4.7, in the form of AZT, 2 times a day for 6 weeks + NVP 1 time a day for 6 weeks, regardless of whether they receive artificial feeding or breastfeeding).

The WHO places on national health authorities the responsibility for deciding whether to recommend to stop or continue breastfeeding for HIV-positive women while on ART (Chapter 4.4.8); in Belarus, "during pregnancy, an infectious disease doctor and an obstetrician-gynecologist, and after childbirth, a neonatologist consults a patient with HIV infection about the risk of MTCT of HIV during breastfeeding and informs about the need for artificial feeding … that the provision of adapted milk formulas for children, those born to HIV-positive women in the first year of life, are provided free of charge" (the CP PMTCT HIV, Chapter 8 and Appendix 4).

If the mother receiving ART continues to breastfeed in Belarus (according to the CP PMTCT HIV 2018, Chapter 8), the child receives NVP once a day for a total of 12 weeks, and only if the risk of HIV transmission is high (the established virus suppression of the in the pregnant woman has not been achieved in 4 weeks before childbirth, HIV infection of a woman during pregnancy or breastfeeding, who received only emergency prophylaxis during childbirth or did not receive it at all, or who interrupted ART during breastfeeding), it possible the same regimen or AZT is prescribed 2 times a day + NVP 1 time per day for a total of up to 12 weeks, or until viral suppression in the mother is achieved, or until breastfeeding is discontinued plus 1 week, but not more than 6 months, which is generally in line with the 2016 WHO Guidelines (Chapter 4.4.7). If a woman is diagnosed with HIV in childbirth or the postnatal period, "ART should be initiated as soon as possible" (the CP PMTCT HIV 2018, Chapter 8); this is in line with the good practice of the 2016 WHO Guidelines, "in high risk of mother-to-child transmission, besides, to provide complementary prophylaxis for the infant, ART should be initiated urgently in all pregnant and breastfeeding woman, even if infection is detected late in pregnancy or after childbirth, because the most effective way to prevent mother-to-child transmission of HIV is to reduce maternal viral load (Chapter 4.4).

20 Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States. https://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf

Part 4. Antiretroviral therapy regimens

Access to therapy

The CP HIV 2017 guarantees ART as a standard of healthcare. ART in Belarus is provided only free of charge[21] and only in healthcare facilities. It is not possible to purchase ARVs at drug stores using your own funds. ART (as routine health care) is provided only to citizens and persons with a residence permit. Normative acts regulate the provision of ART for persons in PDL[22].

For the first time, the 2016 WHO Guidelines declared that ART should be initiated in all adults, pregnant women, children, and adolescents, regardless of the clinical and immunological stage (chapter 4.3). Universal access to ART in Belarus has been declared since January 1, 2018 (the CP HIV 2017, p. 6.1), in reality, it started in mid-2017. Taking into account the phasing of the transition from the previous recommendations to universal access, the priority of the procedure for providing ART for certain categories of PLHIV was declared (which generally corresponded to those mentioned in the 2016 WHO Guidelines, first of all, identifying people with the progression of HIV infection according to the clinical picture up to 3-4 stages and to reducing the CD4 count to the level of severe immunodeficiency), and currently, ART is provided to all PLHIV.

The CP HIV 2017 (Paragraph 8, as well as Annex 5, Tables 1 and 7) includes the 2016 WHO Guidelines on early initiation of ART in adults and children with TB co-infection: during the first 8 weeks of anti-TB treatment, and at CD4 count <50 cells/mm3 during the first 2 weeks (Chapter 4.3), including in patients with MDR-TB co-infection requiring a second-line anti-TB drugs (Chapter 5.2.2).

List of drugs included in the recommendation

The list of drugs recommended by the CP HIV 2017 complies with the WHO protocols, and it is wider than the list of drugs registered in Belarus and included in the restrictive lists of the MoH - the Essential Medicines List[23] and the Republican Formulary of Medicines[24] (see Table 4.1). In practice, the lack of the drug registration in Belarus or the lack of the drug mention in the “restrictive lists” was not a barrier to their purchase and provision to patients.

21 The list of diseases that give citizens the right to free provision of medicines, dispensed by prescriptions of doctors within the essential medicines list, providing outpatient treatment, as well as medical nutrition. Resolution of the Council of Ministers of RB, dated November 30, 2007, No. 1650 (as amended by the Resolution of the Council of Ministers of RB, dated October 23, 2009, No. 1390). Paragraph “Disease caused by human immunodeficiency virus (ICD code B20-B24)”.
22 Resolution of the MoH of RB and the MIA of RB, dated July 07, 2016, No. 82/186 “On additional measures for the provision of medical care to HIV-infected patients in medical units of the criminal-executive system, medical and labor dispensaries of the Ministry of Internal Affairs of the Republic of Belarus and state healthcare organizations.” http://minzdrav.gov.by/ru/dlya-spetsialistov/normativno-pravovaya-baza/baza-npa.php?ELEMENT_ID=6340
23 The essential medicines list. Annex to the Resolution of the MoH of RB, dated August 13, 2018, No. 65 “On amendment of the Resolution of the Ministry of Health of the Republic of Belarus, dated July 16, 2007, No. 65”. Table 2. http://minzdrav.gov.by/upload/dadvfiles/ !Постановление%20М3%20РБ%20от%2013.08.2018%20№%2065.pdf
24 On the establishment of the Republican Formulary of Medicines for 2018. Resolution of the MoH of RB, dated April 03, 2018, No.33. http://pravo.by/document/?guid=3961&p0=W21833004

Table 4.1. Lists of ARV-drugs included in regulatory documents and registered

Class of ARVs	ARV-drugs included in			ARVs registered in RB [2019]
	Essential Medicines List [2018]	Republican Formulary of Medicines [2018]	CP HIV [2017]	
NRTI	TDF ABC 3TC AZT	TDF ABC 3TC AZT	TDF ABC 3TC AZT	TDF ABC 3TC AZT
NNRTI	EFV NVP	EFV NVP	EFV, EFV400 NVP ETR	EFV NVP
PI	LPV/r DRV RTV	LPV/r DRV RTV	LPV/r DRV RTV ATV ATV/r	LPV/r DRV RTV
INSTI	-	-	DTG RAL	DTG
FDC	TDF/FTC AZT/3TC TDF/FTC/EFV	TDF/FTC AZT/3TC ABC/AZT/3TC TDF/FTC/EFV	TDF/FTC TDF/3TC ABC/3TC AZT/3TC TDF/FTC/EFV TDF/3TC/EFV AZT/3TC/NVP	TDF/FTC ABC/3TC AZT/3TC TDF/FTC/EFV

First-line ART regimens according to the 2016 WHO Guidelines

First-line ART regimens in Belarus are largely in line with the 2016 WHO Guidelines (see tables 4.2 and 4.3). The CP HIV 2017 defines that "the ART regimen consists of a combination of the regimen backbone represented by two NRTIs and a third drug of one of three classes: NNRTI, PI or INSTI" (in the WHO Guidelines, the first-line regimen is based on NNRTI or INSTI only). EFV-based first-line regimens are preferred for adults, adolescents, and children over 3 years old, and the preferred NRTI is the TDF + FTC (or 3TC) combination but not the AZT combination (as in the 2016 WHO Guidelines).

The preferred first-line regimen TDF + 3TC (or FTC) + EFV is given without the additional definition of "fixed-dose combination" in the WHO Guidelines. Nevertheless, it is said that "when choosing a treatment regimen, preference is given to prescribing combined drugs in fixed dosages, and regimens with the least number of doses per day are used which improves adherence to treatment" (p. 12), which is in line with WHO Guidelines (Chapter 4.4. 2).

Unlike the 2016 WHO Guidelines, DTG-based regimens are not classified as alternative regimens; they are listed in the "acceptable" section, that is, "when, for reasons of intolerance, clinical contraindications to use, drug interactions, it is impossible to apply any of the preferred or alternative regimens."

In the CP HIV 2017, the ART regimens consist of names of the drugs without specifying their dosage, and also, the possibilities or recommendations for using EFV400 are not emphasized.

Nevertheless, Table 1 "ARV-drugs, basic information" from Annex 3 of the protocol, EFV tablets were mentioned not only in a dosage of 600 mg but also in a dosage of 400 mg with the note: "not used in pregnant women, as well as in patients over 18 years old who take rifampicin";

the combination TDF/FTC/EFV tablets at a dosage of 300/200/400 mg and TDF/3TC/EFV at a dosage of 300/300/400 mg are also mentioned. That is, theoretically, the national protocol leaves the option of choosing EFV at a dosage of 400 mg for initial therapy but it does not insist on this.

The WHO recommendation to stop using d4T in first-line ART regimens due to its toxic effect was implemented long before the approval of the current version of the national protocol; at least since 2015, d4T has not been used in Belarus.

As in the 2016 WHO Guidelines (Chapter 4.4.4), for children 3-10 years old, the ABC + ZTS combination is more preferable than AZT (or TDF) + ZTS (or FTC); the preferred NNRTI is EFV, and the alternative one is NVP.

As in the 2016 WHO Guidelines (Chapter 4.4.5), for children under 3 years old, the preferred NRTI combination is ABC (or AZT) + 3TC, the preferred third drug is LPV/r (regardless of NNRTI use in the past), and the alternative one is NVP. If tuberculosis occurs in children under 3 years old while taking an ART regimen with NVP or LPV/r, it is recommended to temporarily switch to the ABC + 3TC + AZT regimen (and return to the original regimen after completing tuberculosis therapy). The CP HIV 2017 indicates this option as acceptable.

Having co-infection with tuberculosis, in case of mycobacterium sensitivity to rifampicin in adults and children over 3 years old, a regimen with EFV is used. If the use of EFV is not possible, it is possible to use LPV/r in a double dose (for adults, 800/200 mg 2 times a day) or DTG in double dose (for adults, 50 mg 2 times a day) or RAL (for adults, 800 mg 2 times a day); the ABC + 3TC + AZT regimen is used for children under 3 years old (the CP HIV 2017, Annex 3, Tables 12 and 13).

Table 4.2. First-line ART regimens, according to the CP HIV 2017 (Annex 3, Tables 5 and 6)

Regimens	Adults and children 10 years and older	Children 3-10 years old with a body mass <35kg	Children under 3 years old
Preferred	TDF + FTC (or 3TC) + EFV	ABC/3TC + EFV	ABC (or AZT3) + 3TC + LPV/r
Alternative	TDF + FTC (or 3TC) + NVP AZT + 3TC + NVP (or EFV)	ABC/ZTS + NVP AZT/3TC3 + EFV (or EFV) TDF2 + 3TC (or FTC2) + EFV (or NVP)	ABC/3TC + NVP4 AZT/3TC3 + NVP4
Acceptable1	ABC + 3TC + NVP (or EFV) ABC (or AZT3) + 3TC + LPV/r (or ATV/r2) TDF + FTC (or 3TC) + LPV/r (or ATV/r2) TDF + FTC (or 3TC) + DTG	-	ABC (or AZT3) + 3TC + RAL2 ABC + 3TC + AZT5

Notes:
1 Regimens that are acceptable under certain conditions, that is, when, for reasons of intolerance, clinical contraindications to use, drug interactions, it is impossible to apply any of the preferred or alternative regimens.
2 Not registered in Belarus at the time of writing: ATV/r, RAL, TDF, and FTC mono-preparations; according to instructions for use, the use of some ARV-drugs in children is limited by age and body weight.
3 ABC is the preferred NRTI, AZT is prescribed only if allergic reaction and hypersensitivity to ABC is established.
4 NVP regimens are preferred in infants in the first 2 weeks of life.
5 3-NRTI regimen is used for active TB or other special circumstances.

The CP HIV 2017 includes simplified tables on ARV drug dosing in children (adapted from WHO 2017 Guidelines[25]), including the use of dispersible tablets.

Table 4.3. First-line ART regimens, according to the 2016 WHO Guidelines (Tables 4.2, 4.3, 4.5, 4.7)

Regimens	Adults	Adolescents	Children 3-10 years old	Children under 3 years old
Preferred	TDF + 3TC (or FTC) + EFV	TDF + 3TC (or FTC) + EFV	ABC + 3TC + EFV	ABC or ZT + 3TC + LPV/r
Alternative	AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + DTG TDF + 3TC (or FTC) + EFV400 (or NVP)	TDF (or ABC) + 3TC (or FTC) + DTG TDF (or ABC) + 3TC (or FTC) + EFV400 ABC (or AZT) + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + NVP	ABC + 3TC + NVP AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + EFV (or NVP)	ABC or AZT + 3TC + NVP
Under special circumstances	Regimens containing ABC and boosted PI	Regimens containing boosted IP	-	ABC or AZT + 3TC + RAL

Modification of regimens

The national protocols provide for a mechanism to optimize the scheme to increase its effectiveness and safety (the CP HIV 2017, p. 13). Optimization of the regimen can have both individual benefits (for example, reduced frequency of administration, use of combined drugs or drugs with lower metabolic consequences of long-term use), and programmatic benefits (for example, no need to adhere to the cold chain for storage, reservation of PIs for second-line ART regimens). Optimization of ART regimens in children (Table 14 of the CP HIV 2017) includes their simplification and harmonization (overlap with regimens for adults) and may include the switch of LPV/r to NVP or EFV, the switch of AZT to ABC or TDF, the switch of ABC to TDF (for adolescents weighing more than 35 kg), the switch of NVP to EFV (especially at the age of 3 years and older). The 2016 WHO Guidelines also recommend to change of LPV/r to EFV in children who have reached 3 years after virological suppression (Chapter 4.4.5).

Switch to DTG and EFV400 in first-line regimens

The 2018 WHO Guidelines offer this as an alternative option, while the 2019 WHO Guidelines already make DTG a preferred drug in first-line ART regimens. The EFV400 regimen is called the alternative first-line regimen in the 2019 WHO Guidelines.

The Guidelines emphasize that “not all countries can make the transition equally quickly”. Among factors that can influence the rate of transition, there is the availability of generics and inclusion in national guidelines (the 2019 WHO Guidelines, Fig. 1).

DTG is included in the CP HIV 2017 with recommendations for use according to fairly limited indications:

25 WHO Technical Update. Transition to new antiretroviral drugs in HIV programmes: clinical and programmatic considerations (July 2017). https://www.who.int/hiv/pub/toolkits/transition-to-new-arv-technical-update/en/

- As an acceptable first-line ART regimen in adults and children 10 years and older, “when, due to intolerance, clinical contraindications to use, drug interactions, it is impossible to apply any of the preferred or alternative regimens” (Tables 5 and 6 of the Protocol);
- As an alternative second-line regimen in adults and children 10 years and older if EFV or NVP, or LPV/r or ATV r is ineffective (Tables 8 and 9);
- As a third-line regimen in adults and children 10 years and older with the ineffectiveness of EFV and PI drugs (Tables 10 and 11);
- As an ART regimen used in special cases: when HIV and active tuberculosis are combined in patients aged 10 and older when mycobacterium is sensitive to rifampicin and EFV cannot be used (Table 12).

DTG is not included in the Essential Medicines List [2018] and Republican Formular of Medicines [2018].

Moreover, the objective obstacles to follow the WHO recommendations for switching to new drugs are the following: the inclusion of DTG in the preferred first-line regimens is limited in Belarus because of the patent protection of the drug and its corresponding high cost (2,160 USD for an annual course of DTG versus 36 USD for the annual course of EFV600 in 2018), the lack of registration of EFV400 and RAL drugs in Belarus, the impossibility of importing a generic DRV/r in the form of a thermostable fixed combination due to the effect of patent protection on a thermostable RTV.

The WHO recommends a wide transition to first-line DTG regimens, both for new ART beginners and for those already receiving a first-line regimen based on other drugs. Children are advised to switch to DTG when their weight is> 20 kg, when a standard 50 mg tablet can be used once a day (research data supporting this dosing regimen should be published in 2019), whereas the current national HIV CP 2017 (Annex 3) regulates the use of DTG only in children of 12 years and older weighing ≥40 kg. For children, the WHO Guidelines also provide for the optimization of regimens with the transition to TDF when the weight is> 30 kg, and the transition from AZT to ABC to reduce the daily number of tablets in the regimen and maintain the advantages of the NRTI transition procedure (to avoid the accumulation of TAMs when using AZT), which is approximately meets the above-mentioned national guidelines (see Tables 4.4 and 4.5, adapted from the WHO 2019 guidelines).

Table 4.4. Considerations for transition to TDF + 3TC + DTG among adults and adolescents (Table 3 of the 2019 WHO Guidelines)

Treatment transition scenario	Preferred approach	Comments
DTG for people living with HIV initiating ART		
Adults and adolescentsa	Initiate TDF + 3TC + DTG	• Potential risk of neural tube defects among infants exposed to DTG during the conception period • Women not using or accessing contraception or who want to be pregnant can use DTG or EFV based on an informed choice of the risks and benefits of each regimen
Pregnant and breastfeeding womenb	Initiate TDF + 3TC + DTG	• Possibility of conception during breastfeeding remains
TB coinfection	Initiate TDF + 3TC + DTG (DTG dose adjustment needed)	• DTG 50 mg twice daily if rifampicin is being used as the anti-TB regimen
DTG for people living with HIV already using a first-line ART regimen		
Clinical or immune failure or viral load not suppressed	Switch to AZT + 3TC + DTG or PI/rc	• No evidence to support the efficacy of DTG when used in combination with an inactive NRTI backbone • Provide adherence support
Viral load suppressed	Substitution to TDF + 3TC + DTG may be considered according to national recommendations	• Substitution should be considered in the context of drug supply and patient choice • Substitution may confer new side-effects and interfere with adherence • DTG regimens may be more durable in the long term
Clinically and immunologically stabled and viral load unknown	Give priority to viral load testing or consider other programmatic or clinical indications for substitution to DTG based ART	• No evidence to support the efficacy of DTG when used in combination with an inactive NRTI backbone • Provide adherence support
Stabled on suboptimal first-line ART regimens	Substitute to TDF + 3TC + DTG	• Substitution may confer new side-effects. • Provide adherence support

Notes:
aEffective contraception should be offered to adult women and adolescent girls of childbearing age or potential. DTG can be prescribed for adult women and adolescent girls of childbearing age or potential who wish to become pregnant or who are not otherwise using or accessing consistent and effective contraception if they have been fully informed of the potential increase in the risk of neural tube defects (at conception and until the end of the first trimester).
bIf women identify pregnancy after the first trimester, DTG should be initiated or continued for the duration of the pregnancy.
cAfter adherence check and persistent detectable viral load.
dDefined as stable based on national guidelines.

Table 4.5. Considerations for transition to optimal ART regimens for children who are considered stable on ART based on national guidelines (Table 4 of the 2019 WHO Guidelines)

Current regimen	Weight	Optimal regimen for transition	Considerations
AZT + 3TC + NVP AZT + 3TC + EFV ABC + 3TC + NVP	<20 kg	ABC + 3TC + LPV/r	If stable, children can be transitioned to DTG when they reach 20 kg
	20-30 kg	ABC + 3TC + DTG	If stable, children can be transitioned to TDF + 3TC + DTG when they reach 30 kg
	>30 Kg	TDF + 3TC + DTG	-
ABC + 3TC + EFV	<20 kg	No change until they reach 20 kg unless treatment failure occurs	Transition to optimal regimens for these children is of value once they reach 20 kg and DTG can be used maintaining once-daily administration
	20-30 kg	ABC + 3TC + DTG	If stable, children can be transitioned to TDF + 3TC + DTG when they reach 30 kg
	> 30 kg	TDF + 3TC + DTG	-
ABC + 3TC + LPV/r AZT + 3TC + LPV/r	<20 kg	No change until they reach 20 kg unless treatment failure occurs	Ensure the use of tablets as soon as possible to reduce the pill burden. Transition from AZT + 3TC + LPV/r to ABC + 3TC + LPV/r can also be considered to reduce the pill burden and preserve the antiviral advantage of NRTI's sequencing
	20-30 kg	ABC + 3TC + DTG	If stable, children can be transitioned to TDF + 3TC + DTG when they reach 30 kg
	> 30 kg	TDF + 3TC + DTG	-

Monitoring the response to ART and identifying treatment failures

According to the 2016 WHO Guidelines (Chapter 4.5.1), if the patient is on stable ART, then "routine VL monitoring can be performed after 6, 12 months, and then every 12 months to synchronize it with routine monitoring". The CP HIV 2017 follows such recommendations in a similar way, with more frequent monitoring at the beginning of treatment and at low CD4 lymphocyte counts and a transition to rarer monitoring when therapeutic remission is achieved (see Table 4.6).

Following the 2016 WHO Guidelines, national guidelines define virological treatment failure (failure to achieve and maintain viral suppression) as the detection of HIV VL> 1000 copies/ml in two consecutive tests with the interval of ≥3 months apart in the patient on the current ART regimen ≥6 months (the CP HIV 2017, p. 3).

Belarus does not follow the WHO Guidelines on the possibility to stop monitoring the CD4 lymphocyte count "if the state is on stable ART and undetectable viral load", probably because of the risk of missing a possible deterioration in the patient's condition, given the fairly constant availability of tests to determine the CD4 lymphocyte counts in the last years. In the context of the developed logistics of blood collection and delivery to laboratories, Belarus does not collect a dry drop of venous or capillary blood but this option can be considered for implementation in community-based services.

Table 4.6. Laboratory monitoring of ART effectiveness, according to the CP HIV 2017 (Annex 4, Table 2)

Observation period	Viral load	CD4 lymphocyte count1
Before initiating ART	Once before initiating ART	Once every 6 months
After initiating [re-initiating] ART before therapeutic remission*	Once every three months when initiating ART or switching to subsequent series regimens; [after re-initiating of NNRTI-containing regimens: after 1, 3 and 6 months, then once every 3 months until therapeutic remission is achieved]	Once every 6 months (with CD4> 200 cells/mm3); Once every 3 months (with CD4 <200 cells/mm3)2
On ART in therapeutic remission*	Once every 6 months; when detectable VL HIV appears, control after 1 month with adherence counseling and assessment of possible drug interactions	Once every 12 months (with CD4> 200 cells/ mm3); Once every 6 months (with CD4 <200 cells/ mm3)3

Notes:
** Criteria for therapeutic remission: stable viral suppression (undetectable HIV VL twice with an interval of ≥6 months), restoration of immunity sufficient to protect against the emergence of new and progression of existing opportunistic diseases, receiving ART for at least 1 year, no pregnancy or immunosuppressive treatment for other diseases;*
1 When HIV VL is undetectable, the CD4 lymphocyte count is conducted with the frequency prescribed for determining the HIV VL;
2Monitoring of the CD4 lymphocyte counts 1 time in 3 months is carried out to timely terminate the preventive treatment of opportunistic infections;
3 In patients with a stable lack of immunological response with viral suppression for> 6 months, it is permissible to monitor the CD4 lymphocyte counts once every 6-12 months.

Second-line regimens

In Belarus, approaches to switching the ART regimens in case of its ineffectiveness are generally consistent with the WHO 2016 Guidelines, Chapter 4.8 (see Tables 4.7 and 4.8):

- Adults and children over 10 years old are advised to switch to PI-based regimens from first-line regimens based on NNRTIs or DTGs (of which thermostable fixed combinations of ATV/r and LPV/r are preferred, the alternative is DRV/r) or from a regimen with NNRTI to the alternative regimen RAL + LPV/r;
- Children under 10 years old are recommended to switch from the PI-based regimens to the RAL regimens or (for children 3-10 years old) to the EFV regimens; from NNRTI-based regimens, as in adults and adolescents, to PI-based regimens (with LPV/r or ATV/r drugs preferred);
- Change of NRTI combination: after failure of TDF (or ABC) + 3TC (or FTC), it is necessary to use AZT + 3TC, after failure of AZT + 3TC, it is necessary to use TDF (or ABC in children) + 3TC (or FTC).

The CP HIV 2017 states that "preference is given to prescribing combined drugs in fixed dosages" (p. 12), and in practice in Belarus, almost exclusively combined NRTIs are used (TDF/FTC, AZT/3TC, and since 2019 + ABC/3TC) for adults and adolescents.

Table 4.7. Second-line ART regimens, according to the CP HIV 2017 (Annex 3, Tables 8 and 9)

The patients	Ineffective first-line regimen	Second-line regimen	
		Preferred	Alternative
Adults and children aged 10 and older	TDF + FTC (or 3TC) + EFV (or NVP) ABC + 3TC + EFV (or NVP)	AZT + 3TC + LPV/r (or ATV/r1)	AZT + 3TC + DRV r (or DTG) RAL1 (or DTG) + LPV/r (or DRV/r)
	TDF + FTC (or 3TC) + DTG2	AZT + 3TC + LPV/r (or ATV/r1)	AZT + 3TC + DRV/r
	AZT + 3TC + NVP (or EFV)	TDF + FTC (or 3TC) + LPV/r (or ATV/r1)	TDF + FTC (or 3TC) + DRV/r (or DTG) ABC + 3TC + LPV/r (or ATV/r1 or DRV/r or DTG) RAL1 (or DTG) + LPV/r (or DRV/r)
	TDF + FTC (or 3TC) + LPV/r (or ATV/r1) ABC + 3TC + LPV/r (or ATV/r1)	AZT + 3TC + DRV/r	2NIOT3 + NVP 2NRTI3 + EFV 2NRTI3 + DTG
	AZT + 3TC + (or ATV/r1)	TDF (or ABC) + FTC (or 3TC) + DRV/r	-
Children under 10 years old	ABC (or AZT4) + 3TC + LPV / r	AZT4 (or ABC) + 3TC + RAL1	
	ABC (or AZT4) + 3TC + LPV / r	ABC (or AZT4 or TDF1,5) + 3TC + EFV (or RAL1)	
	ABC (or TDF1,5) + 3TC (or FTC1) + EFV (or NVP)	AZT2 + 3TC + ATV/r1,6 (or LPV/r)	
	AZT4 + 3TC + EFV (or NVP)	ABC (or AZT4 or TDF1,5) + 3TC (or FTC1) + ATV/r1,6 (or LPV/r)	

Notes:
1 Not registered in Belarus at the time of writing: ATV/r, RAL, TDF, and FTC mono-preparations; instructions for use as well limit the use of some ARVs in children by age and body weight.
2 Based on the results of a molecular genetic study of blood plasma for the presence of drug resistance mutations in HIV RNA.
3 When two fully active NRTIs are used in the regimen, based on the results of a molecular genetic study of blood plasma for the presence of drug resistance mutations in HIV RNA.
4 ABC is the preferred to NRTI, AZT is prescribed only if there is an established allergic reaction and hypersensitivity to ABC.
5 The WHO approved TDF for use in children over 2 years old.
6 ATV/r is used as an alternative to LPV/r in children over 3 months old.

Table 4.8. Second-line ART regimens, according to WHO 2016 recommendations (Table 4.15)[26]

Population		Failing first-line regimen	Second-line regimen	
			Preferred	Alternative
Adults and adolescents		2NRTI + EFV (or NVP) 2NRTI + DTG	2NRTI + ATV/r or LPV/r	2NRTI + DRV/r
Pregnant and breastfeeding women		2NRTI + EFV (or NVP)	2NRTI + ATV/r or LPV/r	2NRTI + DRV/r
Children	Less than 3 years	2NRTI + LPV/r	2NRTI + RAL	Maintain the failing LPV/r-based regimen, and switch to 2NRTI + EFV at 3 years of age
		2NRTI + NVP	2NRTI + LPV/r	2NRTI + RAL
	3-10 years	2NRTI + LPV/r	2NRTI + EFV	2NRTI + RAL
		2NRTI + EFV (or NVP)	2NRTI + LPV/r	2NRTI + ATV/r

Third-line regimens

The WHO encourages the development of national guidelines for switching to third-line ART regimens and advises to include new drugs with minimal risk of cross-resistance to previously used regimens, such as INSTI, second-generation NNRTIs and PIs (the 2016 WHO Guidelines, Chapter 4.8.3). The CP HIV 2017 regulates the use of two INSTI drugs (DTG and RAL) in the third- line regimens, the latest generation NNRTI drugs (for example, ETR) and INSTI with the highest genetic resistance barrier (DRV/r), see Table 4.9.

If there are difficulties in the empirical switch of the therapy regimen based on the recommendations given, it is possible to perform a resistance test. The indications are: 1) virological failure of treatment with a first-line regimen containing PIs if it is impossible to use NNRTI-based regimens; 2) virological failure of treatment with a second- or third-line regimen; 3) all children with perinatal HIV infection (the CP HIV 2017, p. 20).

Table 4.9. Third-line ART regimens, according to the CP HIV 2017 (Annex 3, Tables 10 and 11)

The patients	First-line regimen	Second-line regimen	Third-line regimen
Adults and children 10 years and older	2 NRTI + EFV	2 NRTI + PI	DRV/r + DTG (or RAL1) ± 1-2 NRTI
	2 NRTI + DTG	2 NRTI + LPV r 2 NRTI + ATV/r1	DRV/r + 2NRTI ± NNRTI2
		2 NRTI + DRV/r	Individual selection3
Children under 10 years	2 NRTI + LPV/r	<3 years: 2 NRTI + RAL1	RAL1 + 2 NIOT DRV/r + 2 NRTI DRV/r + RAL1 + 1–2 NRTI
		> 3 years: 2 NRTI + EFV or RAL1	
	2 NRTI + EFV	2 NRTI + ATV/r1,2 or LPV/r	

Notes:
1 Not registered in Belarus at the time of writing: ATV/r, RAL, TDF and FTC monopreparations, instructions for use as well limit the use of some ARVs in children by age and body weight.
2 The latest generation of NNRTIs (e.g. ETR);
3 Based on the results of a molecular genetic study of blood plasma for the presence of drug resistance mutations in HIV RNA.

26 WHO Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - Second edition. 9 June 2016. Available at: http://www.who.int/entity/hiv/pub/arv/arv-2016/en/index.html

Part 5. Prevention and treatment of concomitant infections and diseases

It includes recommendations for the prevention and treatment of coinfections (tuberculosis, hepatitis B and C), opportunistic infections, and concomitant non-infectious diseases.

Tuberculosis

The WHO recommends Xpert MTB/RIF method (instead of standard microscopy, culture, and drug susceptibility analyses) for initial diagnostic testing in adults and children with suspected HIV-associated pulmonary TB, MDR-TB, and TB meningitis; this methods can also be used instead of conventional methods (including standard microscopy, culture or histological analyses) when testing non-respiratory specimens (lymph nodes and other tissues) from patients with suspected extrapulmonary TB (the 2016 WHO guidelines, Chapter 5.2.2). This recommendation is included in the national CP HIV 2017 (Annex 5, Tables 1, 7; Annex 6, Fig. 1), in the CP TB 2018 and the guidelines for the management of health care[27]: two sputum samples are taken for testing [and other biological fluids and tissues are mentioned below], one sample "must be sent for research using rapid diagnostic methods for TB and MDR-TB (GeneXpert, BACTEC MGIT960, LPA)."

The WHO recommends not to use the LF-LAM (urine ELISA for lipoarabinomannan) TB method for routine screening and the diagnosis of active TB, except for its use as a supplementary method in PLHIV with symptoms of pulmonary or extrapulmonary TB and a low CD4 cell count (<100 cells/mm3) or critically ill (having 4 danger signs: respiratory rate> 30 in 1 min, temperature> 39°C, heart rate>120 in 1 min and inability to walk without assistance). This method is not mentioned in the CP HIV 2017.

Under the WHO Guidelines, the CP HIV 2017 contains an algorithm of screening for active tuberculosis in PLHIV (the CP HIV 2017, Annex 6, Fig. 1). The diagnosis of active TB is suggested to be considered unlikely in the absence of symptoms such as cough, fever, weight loss (in children - poor weight gain) and night sweats, as well as in the absence of contact with TB patients; if these symptoms are present, it is recommended to screen for active tuberculosis using the Xpert MBT/RIF. All PLHIV with excluded active TB is recommended to prescribe isoniazid preventive therapy (IPT): regardless of the degree of immunosuppression, including ART, people who have already received TB treatment, and pregnant women. According to the CP HIV 2017 (Annex 5, Table 2; Annex 6, Fig. 1), IPT is prescribed at a dose of 5 mg/kg/day but not more than 300 mg/day for 6 months every 2 years; with acute or chronic liver damage, excessive alcohol consumption, polyneuropathy, pregnancy, the risk of developing adverse reactions from taking isoniazid increases, which requires more careful monitoring of the patient, but is not a contraindication to IPT. The WHO does not stipulate the frequency of IPT; it recommends to conduct IPT routinely for children over 12 months of age (using a dose of 10 mg/kg/day), and for children under 12 months of age, only if there is a TB contact and after a negative TB test.

27 On approval of the instruction on the procedure for provision of anti-tuberculosis assistance to patients with HIV infection. Order of the MoH RB, dated June 04, 2018, No. 573.

The 2016 WHO Guidelines do not specify TB treatment regimens, but note that "TB patients who are HIV positive and TB patients living with high HIV prevalence should receive rifampicin treatment for at least 6 months. The optimal frequency of administration of the drug is daily at the stages of intensive and continued therapy." This recommendation is fully implemented in national protocols.

The WHO recommends using infection control measures for TB management, including administrative guidelines (logistics of the TB detection system, including the use of Xpert MTB/RIF or similar, and patient flow separation), measures for health workers and those who provide health care (testing availability for them and treatment of HIV and TB), the use of respirators (the equivalent of the N95 standard or higher), and special environmental requirements (ventilation and ultraviolet exposure of the air). Similar measures are regulated by national documents, perhaps, except the recommendation to transfer health workers living with HIV to jobs associated with lower risks[28,29].

Viral hepatitis

The 2016 WHO Guideline provides fairly brief coverage of viral hepatitis B and C, but in 2018 a separate WHO guideline on the treatment of CHCV using DAA was released; comparison of recommendations with national ones is given in table 5.1.

Table 5.1. Comparison of recommendations for the treatment of hepatitis C using DAA

	The 2018 WHO Guidelines[30]	The CP HCV 2019[31]
Whom to treat	All> 12 years of age regardless of fibrosis stage	All ≥18 years old
How to treat	Adults ≥18 years: pangenotypic DAA - no cirrhosis SOF/VEL 12 weeks, SOF + DAC 12 weeks, G/P 8 weeks, with cirrhosis SOF/VEL 12 weeks, G/P 8 weeks, SOF + DAC 12 or 24 weeks Adolescents 12-17 years old or weighing ≥35 kg: SOF/LED 12 weeks (for genotypes 1,4,5,6), SOF + RBV 12 weeks (genotype 2), SOF + RBV 24 weeks (genotype 3) Children <12 years of age: delay treatment until 12 years of age, refuse IFN completely	Using SOF/LED, PrOD, SOF + DAC, SOF/VEL, SOF, RBV

Hepatitis C in adults is not included in the List of diseases that give the right to free provision of drugs[32], however, since 2017, a program on provision free treatment for hepatitis C with direct-acting drugs has been developing. In 2019, the Clinical Protocol was approved, a national program on the elimination of hepatitis C was prepared and is in the process of approval. Co-infection with HIV and hepatitis C (as recommended by the WHO) is identified in the list of priority treatment situations. The lists of pre-treatment check-ups before DAA and screening for the monitoring of the efficacy and safety of antiviral treatment (Tables 4 and 5 of the Protocol) are broader than the WHO recommendations suggesting that the use of pangenotypic combinations eliminates the need for genotyping before initiation of treatment;

28 Sanitary norms and rules "Sanitary and epidemiological requirements for the structure, equipment and maintenance of anti-tuberculosis health organizations and for the implementation of sanitary and anti-epidemic measures aimed at preventing the spread of tuberculosis in anti-tuberculosis health organizations." Approved by Order of the MoH RB, dated June 28, 2013, No. 58. https://www.gotkb.by/documents/norm_akt/28.06.2013%D0%B3%E2%84%9658.pdf
29 Methodological guide "Measures for infection control in anti-tuberculosis organizations". Approved by Order of the MoH RB, dated December 11, 2009, No. 1151. https://www.gotkb.by/documents/norm_akt/1.12.2009%D0%B3%E2%84%961151.pdf
30 The WHO guidelines for the care and treatment of chronic hepatitis C virus infection (2018). http://www.euro.who.int/__data/assets/pdf_file/0006/393711/9789289053891-rus.pdf?ua=1
31 Clinical protocol "Diagnosis and treatment of patients (adults) with chronic viral hepatitis B and C." Approved by Directive of the MoH RB, dated March 19, 2019, No. 19. http://pravo.by/upload/docs/op/W21934091p_1557781200.pdf
32 Перечень заболеваний, дающих право гражданам на бесплатное обеспечение лекарственными средствами, выдаваемые по рецептам врачей в пределах перечня основных лекарственных средств, при амбулаторном лечении, а также лечебным питанием. Постановление Совета Министров РБ от 30.11.2007 г. No 1650 (в редакции постановления Совета Министров РБ 23.10.2009 г. No 1390).

because of limited resources, indirect definition the degree of liver fibrosis is possible with simple tests (APRI, FIB-4); laboratory monitoring of DAA toxicity can be focused on a blood test at the beginning and the end of treatment and the indicator of the effectiveness of the course of DAA treatment is a sustained virologic response 12 weeks after completion of treatment.

Hepatitis C in children under 18 years old is included in the List of diseases that give the right to free provision of drugs, but the children's Clinical Protocol[33] recommends not to use DAA (including SOF and SOF/LED for children ≥12 years of age) but to use pegylated interferon in children over 3 years of age, including in combination with RBV.

Opportunistic infections

The 2016 WHO Guidelines specify TMP/SMX prevention and cryptococcal infection prevention and treatment. The CP HIV 2017 includes detailed recommendations for the prevention and treatment of a wider range of OIs in adults older than 18 years (Annex 5, Tables 1, 2) and in children younger than 18 years (Annex 5, Tables 7, 8): Pneumocystis pneumonia, toxoplasmosis, MAC infection, candidiasis, cryptococcosis, CMV-infection, HSV-infection and some others (cryptosporidiosis, Kaposi's sarcoma, Burkitt's lymphoma, primary CNS lymphoma or B-cell non-Hodgkin's lymphoma, progressive multifocal leukoencephalopathy, HIV encephalopathy, and HIV encephalitis).

TMP/SMX prevention

Indications for starting and stopping the TMP/SMX prophylaxis are given in Table 5.2.

Table 5.2. Indications for starting and stopping the TMP/SMX prevention

Indications	WHO 2016	CP HIV 2017/CP PMTCT HIV 2018
To start	Adults (including pregnant women) with clinical stage 3 or 4 and/or CD4 ≤350 cells/mm3 All PLHIV with active TB regardless of CD4 count Children and adolescents: everyone, regardless of stage (priority for children <5 years old and children with 3 or 4 clinical stages and/or CD4 ≤350 cells/ mm3) HIV-exposed: from 4-6 weeks	Adults with CD4 count <200 cells/ mm3(or <14%) All PLHIV with active TB regardless of CD4 count Children 6-12 months old with each episode of any respiratory infection at the time of its acute manifestations, regardless of CD4); children 1-6 years old with CD4 <500 cells/ mm3 (or <15 %); children ≥6 years old with CD4 count <200 cells/ mm3 (or <15%) HIV-exposed: from the moment of withdrawal of ARV prophylaxis or the 5th day of life (if ARV prophylaxis has not been started)
To stop	Adults (including pregnant women), stable on ART, with restored immunity and suppressed VL Children 5 years and older (in settings with a low prevalence of malaria and severe bacterial infections) with the clinically stable condition and/or achieved virologic suppression on ART for ≥6 months and with CD4> 350 cells/mm3 HIV-exposed: before exclusion of HIV infection based on an appropriate HIV test, after cessation of breastfeeding	Adults: after CD4 count> 200 cells/ mm3 for ≥3 months Children: restoration of immunity on ART (when determined twice with an interval of ≥3 months) - up to one year CD4> 15%, at 1-6 years CD4> 500 cells/ mm3 (or> 15%), > 6 years CD4> 200 cells/ mm3 (or> 15%) HIV-exposed: up to 6 months or two HIV DNA negative (PCR) tests after cessation of breastfeeding

33 Клинический протокол диагностики и лечения пациентов (детское население) с инфекционными заболеваниями при оказании медицинской помощи в амбулаторных и стационарных условиях районных, областных и республиканских организаций здравоохранения Республики Беларусь (утв. Приказом МЗ РБ от 24.08.2012 г. No961)

Due to unavailability in Belarus of alternatives to TMP/SMX (pyrimethamine, sulfadiazine, and pentamidine are not registered and are not available on the market), it is significant to use desensitization regarding TMP/SMX in case of allergic reactions to the drug; for example, in the CP HIV 2017, desensitization regimens related to TMP/SMX of various duration, depending on the necessary urgency of the drug use (Annex 5, Tables 3, 4, 5); dapsone is indicated as an alternative in case of a severe hypersensitivity reaction to TMP/SMX.

The CP HIV 2017 does not provide for the prophylactic prescription of TMP/SMX to all children and adolescents, regardless of the stage of HIV infection (as suggested by the WHO 2016 protocol): one prescribes TMP/SMX in children 6-12 months old for each episode of any respiratory infection during its acute manifestations; children older than one year, only with severe immunosuppression (with CD4 <15%).

Cryptococcal infection

According to the 2016 WHO Guidelines (Chapter 5.3.2), the preferred method for diagnosing extrapulmonary cryptococcosis is “immediate lumbar puncture with CSF pressure measurement and performing a rapid test for cryptococcal antigen (CrAg) in CSF or serum (LA or LFA)”. National recommendations (the CP HIV 2017, Annex 5, Tables 1 and 7) suggest microscopic examination and culture of CSF for cryptococcus (Cryptococcus neoformans) or determination of cryptococcal antigen in the blood, and only at the level of regional and republican health organizations. Harmonization of national protocols under the WHO guidelines (inclusion of a rapid test for a cryptococcal antigen) would allow for the rapid diagnosis of cryptococcal meningitis in healthcare facilities of any level, including the district one.

The CP HIV 2017 does not provide for primary prevention of extrapulmonary cryptococcosis (Annex 5, Tables 2 and 8). For proactive therapy of cryptococcal meningitis in adults (the WHO also recommends for children), when the cryptococcal antigen is detected in the blood and its absence in CSF, fluconazole 800 mg per day is prescribed for 2 weeks, then 400 mg per day for 8 weeks (Annex 5, Table 2). At the same time, it is not implemented the WHO recommendation that considers routine screening for CrAg in blood before ART initiation in adult patients with CD4 lymphocyte count <100 cells/mm3. The prevalence of cryptococcal antigenemia in the population of Belarus has not been studied.

Table 5.3. Treatment regimens for extrapulmonary cryptococcosis, including cryptococcal meningitis (in order of priority according to effectiveness)

Phase	WHO 2016	CP HIV 2017
Induction (at least 2 weeks)	Amphotericin B plus flucytosine; or Amphotericin B plus fluconazole; or A short course of amphotericin B (5-7 days) + high-dose fluconazole (until induction is complete) if minimal complex cannot be administered**; High-dose fluconazole plus flucytosine if amphotericin B is not available; or Only high-dose fluconazole if amphotericin B is not available.	Adults: Amphotericin B lipid complex; or Amphotericin B plus fluconazole; or Fluconazole in high doses Children under 18 years: Amphotericin B (or lipid complex) plus flucytosine*; or Amphotericin B (or lipid complex) plus fluconazole

Consolidation (8 weeks)	Fluconazole 400-800 mg per day (children 6-12 mg kg per day) after two weeks of induction with amphotericin B; Fluconazole 800 mg per day (children 12 mg/kg per day) after induction therapy with a short course of amphotericin B or after induction with fluconazole	Fluconazole 400 mg per day (children 8 mg/kg/day)
Supports (secondary prevention)	Fluconazole 200 mg per day (children 6 mg/kg per day)	Fluconazole 200 mg per day per os (for children, fluconazole 6 mg / kg per day, or itraconazole 5 mg / kg per day)
Timing of ART initiation	After 4 weeks of induction and consolidation of amphotericin B with flucytosine or fluconazole, or After 4-6 weeks of treatment with high doses of oral fluconazole	2 weeks after completion of induction, if it is effective, after excluding toxoplasmosis of the brain and active tuberculosis
Timeline of secondary prevention stopping	Adults and children over 5 years old: stable, adherent to ART and maintenance antifungal therapy for at least 1 year, CD4> 100 cells/ mm3 (two counts at 6 months) if viral suppression is present, or> 200 cells/ mm3 if VL cannot be measured Children: under 2 years old are not stopped, at 2-5 years old - criteria are the same as for older ones, but CD4 achievement> 750 cells/ mm3 is required (> 25%) Restart if CD4 falls <100 cells/mm3 (in children 2-5 years old, ≤750 cells/ mm3 or ≤25%), or if stage 4 clinical episode is developed according to the WHO	Adults: at least 12 months if viral suppression is achieved and CD4> 100 cells/ mm3 for at least 3 months Children: age over 6 years old, asymptomatic ≥12 months, with viral suppression and CD4> 100 cells/ mm3 (≥15% in children 1-6 years) for at least 3 months

** Flucytosine is not registered and absent on the Belarusian market*
*** According to the WHO recommendations, the national protocol also includes a minimum set of measures to reduce the serious toxic effects of amphotericin B, including prehydration and electrolyte replenishment (and additionally, prolongation of infusion, use of NSAIDs), as well as laboratory monitoring of hypokalemia and nephrotoxicity*

The treatment regimens and secondary prevention of extrapulmonary cryptococcosis in the national protocols generally comply with the WHO recommendations, except for flucytosine for adults that was not mentioned (the drug is not registered and not available on the Belarusian market), the increased dose of fluconazole for treatment in the consolidation phase is not provided for in case of previous induction with a short course of amphotericin B or fluconazole, and more stringent criteria for stopping secondary prophylaxis in children (over 6 years old). Due to the availability of examinations, the national protocol does not consider situations with the failure to monitor the toxicity of amphotericin B and the failure to determine the viral load. In addition to the standard, the lipid complex of amphotericin B, available in the country, is mentioned.

Concomitant non-communicable diseases

According to the current regulatory document[34], health care for PLHIV in Belarus is provided in public healthcare facilities at the place of residence (place of staying), corresponding to the profile of clinical manifestations of a particular disease, based on current clinical protocols or methods of providing medical care for the profile of a particular disease (Chapter 3, Paragraphs 12, 13).

34 On the approval of the instruction on the procedure for managing health care to persons infected with the human immunodeficiency virus. Resolution of the MoH of RB, dated November 08, 2017, No. 93. http://pravo.by/upload/docs/op/W21732603_1513112400.pdf

This is generally in line with the WHO recommendations: for example, “assessment and control of cardiovascular risk should be conducted for all people living with HIV according to standard protocols recommended for the general population”, and “strategies for the prevention and reduction of the risk of cardiovascular disease by targeting modifiable risk factors such as blood pressure, smoking, obesity, unhealthy diet and lack of physical activity” (WHO 2016, Chapter 5.3.1).

However, PLHIV has a number of specific needs regarding the monitoring and management of concomitant non-communicable diseases. Thus, in the framework of monitoring the health status of PLHIV in Belarus, regular medical examinations (every 6 months), general clinical examinations (general and biochemical blood tests every 6 months, common urine analysis), monitoring side effects of drugs (assessing lipid metabolism disorders annually, the use of TDF - assessment of the glomerular filtration rate by creatinine clearance, the level of total calcium and inorganic phosphorus in the blood every 6 months, but densitometry is not prescribed), registration of an electrocardiogram, a preventive appointment with an obstetrician-gynecologist for women annually (the CP HIV 2017, Annex 4, Table 1).

Recommended by WHO inclusion of “assessment and management of depression” in services for all PLHIV is not mentioned in the CP HIV 2017; only a contraindication to the use of EFV “in patients with severe mental disorders, depression” is defined.

Narcologists provide assistance in the use of psychoactive substances in Belarus, which is regulated by relevant documents.

The specific needs for medical services of the main key populations are not specified (the CP HIV 2017 defines them as PWID, MSM and TG, female CSW, persons in PDL, and migrants).

Part 6. Health services delivery

Continuity between HIV testing and inclusion in HIV treatment and care

The CP HIV 2017 practically does not regulate the issues related to service provision; they are mentioned in the order on the procedure for organizing medical care for PLHIV[35] and some other documents.

The WHO proposes sequential interventions that shorten the time from diagnosis to initiation of treatment, peer support, and ensuring continuity between stages of care. The procedure for the management of the healthcare provision to PLHIV in Belarus is given in Table 6.1; Different documents define it somewhat differently.

Table 6.1. The procedure for providing health care to PLHIV in Belarus

No.	Stage [what is regulated by]	Who conducts, timing
1	Provision of information on test results to the CGE [the CP HIV 2017]	Laboratories, within ≤24 hours
2	Provision of information to the healthcare organization that sent the blood sample for testing, in written form [the CP HIV 2017]	Epidemiologists CGE, within ≤24 hours
3	Crisis counseling and epidemiological investigation, referral to IDO or CDD/ CDO [R № 93]	Epidemiologists CGE, within ≤72 hours
	Post-test counseling [the CP HIV 2017]	A healthcare worker who received the test result
4	Organization of dispensary observation, testing for the CD4 lymphocytes count[R № 93]	Infectious disease physician of IDO or CDD/CDO at the state healthcare facility (if absent - a general practitioner or pediatrician)
5	Clinical staging of HIV infection, prescribing an ART regimen [R № 93]	Infectious disease physician of CDD/ CDO at regional state health healthcare facility, infectious diseases hospitals in Minsk
	Prescribing first-line ART regimens (preferred or alternative) [the CP HIV 2017]	Infectious disease physician of healthcare organizations of the district (city) level
	Prescribing ART regimens in the penitentiary system[36]	Infectious disease physician (if absent, a general practitioner, a primary care physician or a TB specialist who has undergone advanced training)
6	ART delivery, adherence control and laboratory monitoring [R № 93]	Infectious disease physician of IDO or CDD/CDO at the state healthcare facility (if absent - a general practitioner or pediatrician)

Note: R № 93 - Resolution of the Ministry of Health of the Republic of Belarus dated November 08, 2017, # 93.

After testing positive for HIV and before receiving treatment, the person should visit:

- Epidemiologist (for crisis counseling and epidemiological investigation)[37], then
- Infectious disease physician (for registration in a clinic and testing for CD4 counts), then

35 On the approval of the instruction on the procedure for managing health care to persons infected with the human immunodeficiency virus. Resolution of the MoH of RB, dated November 08, 2017, No. 93. http://pravo.by/upload/docs/op/W21732603_1513112400.pdf
36 Instruction on additional measures to organize the provision of antiretroviral drugs. Approved by Order of the MoH RB, dated February 16, 2018, No. 142, Paragraphs 8 and 9.
37 When a patient is in an anti-tuberculosis or other healthcare facility, a visit by an epidemiologist or an assistant to an epidemiologist is organized.

- If a person lives in areas without CDD/CDO (the issue is differently defined in two documents, see Table 6.1), it may additionally require a visit to an infectious disease physician of CDD/CDO at the regional center (for the clinical staging of HIV infection and prescribing an ART regimen), and only then
- Infectious disease physician at IDO or CDD/CDO to receive medications.

It turns out that testing, post-test counseling and the delivery of therapy are conducted in different institutions and by different people: testing by a doctor in a healthcare facility (in reality, also a community consultant at a pint of services), post-test counseling if the result is positive, is provided by an epidemiologist at the CGE, observation, and therapy is prescribed by infectious disease physician at CDD/CDO.

While conducting crisis counseling, the epidemiologist's tasks are rather concentrated not on providing support and establishing subsequent interaction (this meeting will be the first and probably the only one), but on establishing epidemiological data (which could have been done later, not at the stage of post-test counseling) and on the identification of measures one need to comply with to prevent the spread of HIV, including a written warning about criminal liability for knowingly placing at risk of being infected or infecting another person. The recommendation on the pre-and post-test consultation by one person is not followed. A visit to an epidemiologist at CGE (which is often located not close to a healthcare facility, where a person will later be followed up by an infectious disease specialist) may be an excessive link in the chain from testing to receiving treatment.

Possibility to involve peer consultants to work as "representatives of public organizations of people living with HIV and/or HIV service public organizations"[38] is defined in the framework of a multidisciplinary team at CDD (which are organized in regional cities and the city of Minsk with more than 350 registered HIV-positive patients), but not at CDO, IDO (under the supervision of an infectious disease specialist in district cities), and not at CGE (when conducting crisis counseling by an epidemiologist). At the same time, "the participation of representatives of public organizations in MDT is organized within the conclusion of an agreement on the provision of services free of charge during the implementation of international technical assistance projects by a public organization, or in the framework of the state social order in accordance with the current legislation," and their main function is individual work with patients to involve him/her and form the sustainable motivation for follow-up monitoring and treatment, as well as work with the patient's surroundings to improve relationships and increase the patient's level of functioning in the family. The work is carried out with the consent of the patient and his/her relatives, in compliance with confidentiality.

Thus, the implementation of timely involvement in the treatment and care system (the 2016 WHO Guidelines, Chapter 6.4.1), reflected also in the provision of good practice ("efforts should be made to shorten the time between HIV diagnosis and initiation of ART, based on assessing the patient's readiness" (Chapter 4.3.6)), is complicated by the following:

- Non-recognition of RT results for saliva as a screening test (the need for an additional visit to test blood to complete the first stage of testing);

38 On approval of the Instruction on the procedure for organizing the work of the consultative and dispensary department on HIV infection. Order of the MoH RB, No. 715, dated July 17, 2018, http://pmplus.by/press-room/news/715.pdf

- In most cases, it is impossible to determine the CD4 lymphocytes count and viral load already in the second blood sample taken in case of positive ELISA/IB (also the need for an additional visit);
- Testing, post-test counseling and providing the therapy take place in different locations and by different people (the test is performed by a physician or a consultant at a low-threshold service, an epidemiologist is consulted at CGE, and the therapy is provided by an infectious disease specialist at IDO or CDD/CDO);
- Lack of peer consultants in most of IDO or CDD/CDO;
- Failure to dispense the therapy on community-based integrated low-threshold services.

The WHO recommendation for determining the level of CD4 lymphocytes at the point of care (Chapter 6.4.2) has been implemented because blood sampling with its subsequent delivery to the laboratory is carried out in healthcare facilities at the patient's place of residence; no visits to other institutions are required. The transmission of information on the results of laboratory tests in electronic form (Chapter 6.4.3) is not specifically regulated in national documents.

Retention of the patient in the care system, support for adherence to treatment

The CP HIV 2017 defines the terms of retention and withdrawal from treatment, adherence to therapy, indicates that "the correct selection of the first-line regimen and ensuring high adherence to treatment in PLHIV are the key to long-term effective ART with the least adverse effects," and also emphasizes that health care workers "must constantly help the patient maintain high adherence to ART." The protocol does not specifically provide for community support of PLHIV, as well as for the provision of ARV drugs and assessment by non-medical workers in health facilities or community services (the 2016 WHO Guidelines, Chapters 6.5 and 6.6), but as previously mentioned, peer counseling is defined as part of the MDT work at CDD. Among other measures to increase adherence, the CP HIV 2017 defines that "preference is given to the appointment of fixed-dose combination drugs and the use of regimens with the least number of doses per day", but it does not include a number of other WHO recommendations (reminders that sent text messages to the phone, training courses on behavioral skills and adherence, cognitive-behavioral therapy).

Frequency of visits

To a healthcare facility is determined by the need for clinical examinations, laboratory testing (see Table 4.6 of the Report, as well as the CP HIV 2017, Annex 4, Tables 1 and 2) and the receipt of drugs. The WHO recommends a lower frequency of visits to a healthcare facility (after 3-6 months) if the condition is stable on ART, scheduled clinical examinations at the same time as dispensing drugs, and also optimize the supply management system of drugs to ensure their availability and prevent shortages (the 2016 WHO Guidelines, Chapter 6.7). National documents define the number of ARV-drugs given out to the patient as not less than a monthly requirement, "up to 6 months in the absence of side effects and adverse reactions in him/her [the patient] after taking ARV drugs and with high adherence to treatment. In the first 6 months [...] for up to 2 months[39]." Opportunities exist for Patient monitoring of treatment interruptions is possible[40].

39 Instruction on additional measures to organize the provision of antiretroviral drugs. Approved by Order of the MoH of RB, dated February 16, 2018, No. 142, paragraphs 8 and 9.
40 Goloborodko N.V., Statkevich I.E., Khatko V.V. Access to treatment for HIV and hepatitis C in Belarus: an analytical report. BPA "Positive Movement": Minsk, 2019. - 106 p. http://pmplus.by/press-room/news/vich/dostup_k_lecheniyu_vich_infektsii_i_gepatita_s_v_belarusi_novyy_otchet_2019/

Redistribution and delegation of responsibilities

Unlike the WHO guidelines, national regulations do not allow "trained non-medical personnel, midwives and nurses can initiate [and continue] first-line ART" and that ART drugs under the supervision of healthcare workers can be dispensed by "trained lay healthcare workers at healthcare facilities" or in the periods between the planned regular visits of the patient to the healthcare facility, by directly "community representatives"(Chapter 6.8).

National documents do not specifically regulate which professional health worker can dispense drugs, but in practice, nurses at IDO or CDD/CDO sometimes dispense drugs on behalf of a doctor. The work of a multidisciplinary team at CDD is based on the principle of "division of responsibilities among members of MDT to achieve a common goal[41]" but there is no provision for prescribing and/or dispensing drugs by anyone other than a physician (including neither a social worker nor a representative of public organizations).

Decentralization

The procedure for prescribing an ART regimen is somewhat differently defined by different national documents (see Table 6.1 above): The Directive on the procedure for providing care to PLHIV determines that ART can only be prescribed by infectious disease physician of CDD/CDO of regional state healthcare facilities and infectious diseases hospitals in Minsk, and the CP HIV 2017 regulates that the appointment of first-line ART regimens (preferred or alternative) can be performed by infectious disease physician of healthcare facilities at the district (city) level. ART is conducted by infectious disease physicians of IDO or CDD/CDO of the state healthcare facility, and in their absence - by general practitioners or pediatricians. All PLHIV in Minsk are monitored in the same two city CDDs (at adult and children's infectious diseases hospitals), and not in IDOs of clinics at the place of residence or registration.

The option, recommended by WHO, to continue ART at the community level (in outreach work, first-aid centers, home care, and community-led services) is not supported by national documents, although this could be useful for hard-to-reach key populations.

Integration and interaction of services

Following the 2016 WHO Guidelines (Chapter 6.10.2), ART is initiated in "PLHIV in a TB facility, followed by referral to an HIV treatment program". So, when a patient with a previously established HIV-positive status or when a patient with tuberculosis is diagnosed with HIV infection in an anti-tuberculosis healthcare facility, the patient is consulted within 5 days by an infectious disease physician; an infectious disease physician and a TB doctor jointly determine and organize the necessary studies; ART is prescribed in 2-8 weeks after the start of treatment with anti-tuberculosis drugs, the anti-tuberculosis organization provides the patient with ARV-drugs regardless of his/her place of residence or registration; further treatment after discharge is conducted by an infectious disease physician and a TB doctor at the place of the patient's residence or registration[42].

Belarus does not provide for WHO-recommended opportunities for TB treatment in infectious diseases hospitals (Chapter 6.10.2), ART in facilities providing opioid substitution therapy (Chapter 6.10.3), and linking HIV treatment facilities with STI treatment and family planning ones (Chapter 6.10.4), as well as the integration of healthcare services with community-led services.

41 On approval of the Instruction on the procedure for organizing the work of the consultative and dispensary department on HIV infection. Order of the MoH RB, No. 715, dated July 17, 2018. http://pmplus.by/press-room/news/715.pdf
42 On approval of the instruction on the procedure for organizing the provision of anti-tuberculosis care to patients with HIV infection. Order of the MoH RB, dated June 04, 2018, No. 573. pp. 23-27, 34.

Medical services tailored to the specificities of adolescents

According to the 2016 WHO Guidelines (Chapter 6.11), while providing care for adolescents, it is necessary to implement health services with a focus on peculiarities of their groups, including training health workers on the characteristics and needs of this group, conducting community-based activities, and sharing information with adolescents about the potential benefits and risks of disclosing their HIV-status to other people and helping them make decisions about when, how and to whom to disclose, if necessary, this information. National documents do not contain special sections on working with adolescents, except for the specifics of counseling them while testing for HIV[43].

Providing harm reduction services

Sustainable development concept[44] foresees the implementation of harm reduction programs as "measures taken to reduce the negative health consequences associated with behaviors of persons of risk groups, including counseling, provision of protective equipment, psychosocial support, information and educational activities, legal and other types of assistance" by healthcare organizations "in partnership with NGOs and international organizations."

Improving the quality of service- provider's work to respond to HIV infection

HIV care programs should be person-centered and tailored to the needs, preferences, and expectations of individuals and communities, promote respect for human dignity, especially when working with vulnerable populations, and involve patients and their families in making informed decisions about their own treatment; provide timely and appropriate safe and acceptable medical and non-medical services to reduce morbidity and mortality from HIV-related causes, improve overall health and quality of life; promote the efficient and economical use of resources (the 2016 WHO Guidelines, Chapter 6.12, provision of good practice). National documents on HIV infection do not contain separate provisions on comprehensive services and person(family)-oriented care, but this often appears from the context of the documents themselves or is regulated by general documents on health care, for example, the Law "About Health Care". In the framework of the implementation of the state social order, it is envisaged to provide subsidies from local (regional) budgets to non-governmental and non-profit organizations for «the provision of services and implementation of projects to reduce the risk of HIV infection among the most vulnerable groups of the population[45]."

Planning and coordination of actions to combat HIV infection at the national level

Are ensured by the presence of a unified strategy formulated in the above-mentioned subprogram "Prevention of HIV infection" of the State Program "Health of the People and Demographic Security of the Republic of Belarus" and the Concept of sustainable development of the system of prevention, treatment, care and support in connection with HIV/AIDS and tuberculosis, as well as the existence of a unified monitoring and evaluation system through the functioning of the State Register of Patients with HIV Infection and the activities of republican and regional groups for monitoring and assessing the situation with HIV/AIDS.

43 Recommendations for voluntary counseling while HIV testing. N.V. Goloborodko, G.V. Lapitskaya. Instructions for use. Reg. number 134-1211. Approved by the MoH RB December 23, 2011 http://pmplus.by/upload/iblock/356/instruktsiya-dkt.pdf
44 Concept of sustainable development of the system of prevention, treatment, care and support due to HIV/AIDS and tuberculosis. Approved by the Minister of Health of the Republic of Belarus on April 21, 2017. Agreed by the CCM for interaction with the Global Fund (protocol of December 22,2016, No. 58). http://pmplus.by/upload/iblock/14b/kontseptsiya_aprel_2017.pdf
45 Subprogram 5 "Prevention of HIV infection" of the State Program "Health of the People and Demographic Security of the Republic of Belarus" for 2016 - 2020. Appendix 5 to the Resolution of the Council of Ministers of the Republic of Belarus, dated March 14, 2016, No. 200. http://minzdrav.gov.by/dadvfiles/000111_759481_postan200.doc (from page 185)

Part 7. Brief analytical summary

Table 8.1. provides a list and a brief description of the main identified discrepancies between national protocols and WHO recommendations, as well as proposals for their harmonization, taking into account these discrepancies.

Table 8.1. Main identified discrepancies and proposals for harmonization of national protocols with WHO recommendations[46]

No.	Main identified discrepancies of national protocols with WHO recommendations	Proposals for harmonization
Part 1. General block		
1	The issues considered in the WHO recommendations are regulated by a number of national documents; the CP HIV 2017 does not include issues of organizing assistance to PLHIV and some other questions	Include a list of the main current normative documents on HIV as an annex to the national protocol
2	The target audience of the national protocol is defined only as workers of the health care system of Belarus	Add community-led service workers and include appropriate recommendations in the protocol (e.g. on counseling, RT conducted by non-healthcare workers, dispensing ARV-drugs for PrEP)
3	The purposes of the national protocol are not clearly explained	Specify that the protocol is based on specific guidelines and is aimed at the implementation of previously defined national purposes (including those formulated in the profile State Program)
4	Definitions of terms include a number of oversights	Include terminology for PrEP and PEP, point-of-care testing, participation non-medical workers in care, as well as such terms as “integrated services” and “continuum of HIV care”; indicate the relapse of the terms “stable state on ART” (WHO) and “therapeutic remission” (CP HIV)
5	Procedural issues related to creation, dissemination and evaluation of recommendations are not regulated	Indicate the team of authors (including the regulation of conflicts of interest, participation of representatives of patient organizations), a procedure for developing the protocol (using the WHO guidelines and other sources, assessing the quality and strength of the recommendations), as well as a procedure for approving the protocol and a plan for revising the recommendations
Part 2. Diagnostic recommendations		
6	The national protocol introduces restrictions on the use of RT: the diagnostic algorithm includes only RT using blood (but not saliva)	Use the term “rapid test” using for both blood and saliva, since the sensitivity and specificity of RT for blood and saliva are comparable; since the first sample of biological fluid to be tested may be saliva, replace the words “re-taken blood sample” with “repeated sample (blood)”
7	The possibility of testing at the level of community services has not been determined: a primary-positive test is considered only if it is performed “in a healthcare organization”, a repeated sample (blood) is also sent to the laboratory only by a “healthcare organization” (in fact, a limitation not applied in Belarus)	Eliminate this limitation from the testing algorithm by prescribing the possibility of RT taking and blood taking, including at the level of community services, which legitimizes the existing practice
8	Good practice clause of the WHO on the possibility of fingerstick sampling by trained non-laboratory personnel is not included	Enable this possibility, which legitimizes existing practices at the community service level
9	There is no possibility to reduce the testing algorithm for populations with a high HIV prevalence (in Belarus these are PWID, MSM, female CSWs and people in PDL) with confirmation of HIV infection based on two positive tests	The idea of shortening the testing algorithm for key groups seems important; it is necessary to consider for them the possibility of taking a second sample (blood) using not ELISA and IB, but ELISA and VL measuring
10	Voluntary, mandatory and compulsory (not used in real practice) testing is regulated	Eliminate compulsory testing from legislation as inconsistent with WHO documents
11	There are lists of contingents subject to mandatory testing for HIV (there are three existing lists at the same time)	Unify the existing lists of contingents subject to mandatory testing for HIV (for clinical and epidemiological indications); the recommendation to offer “HIV testing to all children, without exception, whose parents are living with HIV” is probably redundant due to the low prevalence of HIV infection among children in Belarus, but could be considered

46 Since Belarus is at the stage of a concentrated HIV epidemic, WHO recommendations for generalized epidemic conditions are not considered here.

12	There are no recommendations on who should be offered voluntary testing (including at the level of community services); voluntariness is considered only as testing at the active request of the client/patient	Create a list of indications for offering voluntary testing in health care facilities and at the level of community services, detailing recommendations for adolescents (including HIV testing in the list of simple medical interventions that can be agreed from the age of 14), couples and partners (including "partners of HIV-infected TB patients"), as well as certain key populations (PWID, MSM, female CSW and people in PDL)
13	There is no specific anti-discrimination legislation on HIV	Consultation with representatives of key populations is required
14	The algorithm for diagnosing HIV infection in children under 18 months of age does not regulate the timing of subsequent serological testing (after excluding HIV transmission by PCR testing) and does not specify the possibility of using RT for these purposes.	Prescribe the first serological examination at the age of 9 months (not younger) and the possibility to use RT for this purpose
15	The minimum thresholds for the sensitivity and specificity of serological and PCR tests for testing infants have not been determined, and the maximum allowable time for the issuance of results has not been determined	Enter the relevant information into the CP HIV
16	Belarus does not follow the WHO recommendations on double testing of all pregnant women (only pregnant women at risk are re-tested, as well as if the partner's HIV status is unknown or in the presence of clinical and epidemiological indications) and about repeated testing seronegative breastfeeding mothers throughout the entire period of breastfeeding	Repeated testing of pregnant women from risk groups only and refusal to test breastfeeding seronegative mothers are associated with a low estimated risk of their infection and does not require revision at the moment
Part 3. ARV drugs for HIV prevention		
17	Issues regarding HIV PrEP and PEP are not regulated in any way	Include in the national protocol recommendations for HIV PrEP and PEP, including indications and regimens for each of the population groups (including MSM and TG, female CSW and discordant couples); envisage in the State Program the purchase of ARV-drugs not only for treating HIV infection and conducting HIV PMTCT but also for PEP and PrEP
18	The logistics of receipt, storage, and distribution of drugs for PrEP and PEP in healthcare facilities is not specified; the possibility of providing drugs on community-run points of services is not stipulated	Specify the logistics in the clinical protocol or in a separate document (since the current order for organizing care concerns only PLHIV directly)
19	A different PEP regimen for the newborn during PMTCT of HIV in situations where the risk of vertical HIV infection is high (pregnant women who received ART for less than 4 weeks or with unreported viral suppression 4 weeks before delivery, or did not receive ART, or are primarily positive for ELISA/ICA, or RT)	This regimen (AZT 6 weeks + 3TC 2 weeks + NVP in the first 6 hours, in 2 and 6 days of life, instead of recommended by WHO AZT + NVP regimen for 6 weeks) is used following the US DHHS Guidelines and does not require changes
Part 4. Antiretroviral therapy regimens		
20	The list of ARV-drugs in the national protocol corresponds to those in the WHO Guidelines but the guarantees of their availability are not met: for example, in 2019, DTG was not included in the current restrictive lists, and EFV400, RAL, ATV, and ATV/r were not included in the current restrictive lists, not registered and were absent in Belarus	Specify guarantees of availability of the drugs mentioned in the clinical protocol and include them in restrictive lists (Essential Medicines List and Republican formulary of medicines)
21	DTG is not included in preferred and even alternative first-line regimens (as recommended by WHO in 2019), but is only used for limited indications: 1) as an acceptable first-line regimen in adults and children ≥10 years of age, "when, due to intolerance, clinical contraindications to use, drug interactions, it is impossible to apply any of the preferred or alternative regimens"; 2) as an alternative second-line regimen in adults and children ≥10 years of age with the ineffectiveness of EFV or NVP, or LPV/r or ATV/r; 3) as a third-line regimen in adults and children ≥10 years old with the ineffectiveness of EFV and PI drugs; 4) as an ART regimen used in special cases: when HIV is combined with active tuberculosis in patients aged ≥10 years when mycobacterium is sensitive to rifampicin and EFV cannot be used.	Include DTG in preferred first-line regimens labeled "subject to affordable quality generics available"

22	EFV is mentioned in the therapy regimens without specifying a specific dosage of the drug, and the table with basic information about ARV-drugs consists of two tablet dosages - 600 mg and 400 mg (and also FDC TDF/FTC/EFV at a dosage of 300/200/400 mg and TDF/3TC/EFV at 300/300/400 mg)	Specify a preferred recommendation for the use of EFV at a dosage of 400 mg, and in combination tablets
23	A preference was declared for prescribing "fixed-dose combination drugs and [regimens] with the least number of doses per day", but in reality, some non-combined NRTIs (ABC + 3TC) are used, and the proportion of 3-in-1 combinations for 2017-2018 was no more than 5 % of all regimens	Include in the national protocol a plan on increase FDC coverage with target values for the proportion of 3-in-1 combinations among first-line regimens (at least among EFV-based regimens)
24	Belarus does not follow the WHO recommendation on the possibility to stop monitoring the level of CD4 lymphocytes in a stable state on ART and undetectable VL	This option is not considered due to the relatively constant availability of tests to determine the level of CD4 lymphocytes in recent years, and a weak correlation between the clinical picture and the level of CD4 lymphocytes
25	Belarus does not regulate the possibility of taking a dry drop of venous or capillary blood for examination within ART monitoring	This option may not be as important in the context of advanced logistics of blood collection and delivery in the laboratory, but it may be considered for implementation in a community-service setting.
Part 5. Prevention and treatment of concomitant infections and diseases		
26	The clinical protocol recommends a 5 mg/kg/day dose of isoniazid for IPT in children, while WHO recommends using 10 mg/kg/day	The dose should be adjusted according to WHO recommendations
27	The recommendation to transfer healthcare workers living with HIV from TB care facilities to work with a lower risk has not been implemented	This recommendation should be discussed with the TB community as it is an ethical issue affecting the autonomy of health care providers.
28	The prophylactic prescription of SMX/TMP is not provided for all children and adolescents, regardless of the stage of HIV infection (children 6-12 months are prescribed for each episode of any respiratory infection during its acute manifestations, children older than one year - only in case of severe immunosuppression)	It is not necessary to follow this WHO recommendation due to the low prevalence of malaria and severe bacterial infections in the region, and due to the easy availability of pediatric care
29	It was not determined that a rapid test for cryptococcal antigen (CrAg) in CSF or serum is the preferred method for diagnosing extrapulmonary cryptococcosis; the clinical protocol equally lists microscopic examination, the culture of CSF for cryptococcus and determination of CrAg in the blood, but only at the regional and republican levels	Determine the rapid cryptococcal antigen test as the preferred diagnostic method, including at the district level
30	The recommendation to consider routine screening for CrAg in blood prior to initiation of ART in adult patients with CD4 lymphocyte count <100 cells/mm3 is not implemented	Assess the prevalence of cryptococcal antigenemia in the population of Belarus, include a recommendation if the prevalence is> 3%
31	The recommendation for proactive therapy of cryptococcal meningitis in children was not implemented (specify only for adults)	Include this recommendation in the protocol
32	It is provided a standard dose of fluconazole for the treatment of extrapulmonary cryptococcosis in the consolidation phase, regardless of induction type	Determine the dose of fluconazole as 800 mg per day (children 12 mg/kg per day) in case of induction with a short course of amphotericin B or fluconazole
33	Discontinuation of secondary prophylaxis of extrapulmonary cryptococcosis in children under 6 years of age is not provided	Specify the possibility to discontinue secondary prophylaxis in children over 2 years of age based on symptomlessness ≥12 months, viral suppression and CD4 lymphocyte count ≥15% for at least 3 months
34	Assessment and management of depression is not included in the package of services for the care of PLHIV	Include a section with recommendations on the mental health of PLHIV in the clinical protocol
35	There are no recommendations on the special needs and peculiarities of providing assistance to adolescents, couples and representatives of key groups (PWID, MSM and TG, female CSW, persons in PDL, and migrants)	Specify special needs and peculiarities of providing assistance to adolescents, couples, and representatives of key groups
Part 6. Health service delivery		
36	Difficulties to implement the WHO good practice provision on continuity and shortening the time between HIV diagnosis and ART initiation	Consider the possibilities: 1) Simplify the testing chain for key groups, including by involving community services (see part 2 above); 2) Specify VL and the CD4 lymphocytes count in the second sample (blood) for representatives of key groups; 3) Combine a territorially completed file of the epidemiological studies by epidemiologist and the first examination by the infectious disease specialist; 4) Involve peer consultants for work at CDD/CDO; 5) Dispense ARV-drugs at community-run point of services

37	The transfer of information in electronic form about the results of laboratory tests is not regulated	Consider this option
38	First-line ART should not be prescribed and administered by trained non-medical staff, midwives, and nurses	The possibility of prescribing ART by nursing staff is not relevant for Belarus due to easy accessibility of a doctor's consultation (an infectious disease specialist, or, in his/her absence, a therapist or pediatrician); Consider to include in regulatory documents the existing practice of dispensing ARV drugs by a nurse based on consultation with a physician if there is no need for a medical examination
39	It is not allowed to dispense ARV drugs by trained lay workers at healthcare facilities, or by community representatives (between planned visits) in outreach, at first aid posts, settings providing home care services and community-run services	This opportunity could be in demand for hard-to-reach representatives of key groups, its implementation should be considered
40	The principles of providing person- (family-) oriented assistance and providing comprehensive services are not defined	These principles should be included in the national clinical protocol.
41	Maintaining treatment retention and adherence is identified only as a task for healthcare providers and not for community representatives	The provision of interventions to maintain adherence by peer consultants (representatives of public organizations) should be prescribed in the clinical protocol and the regulation on CDD (chapter on MDT)
42	Separate interventions on maintaining adherence are not identified	Consider the inclusion of WHO-recommended interventions such as reminders that send text messages to the phone, behavioral and adherence training, cognitive behavioral therapy
43	Treatment of tuberculosis in infectious diseases hospitals, dispensing of ART at facilities providing opioid substitution therapy, joining HIV treatment facilities with STI treatment services are not provided	The option of treating tuberculosis in infectious diseases hospitals is not relevant for Belarus, since there is a separate TB service, and not all infectious diseases hospitals can provide the required anti-TB infection control measures (for example, wards with exhaust ventilation); the issue of dispensing ARV drugs in institutions providing opioid substitution therapy should be considered, at least for force majeure situations when the client cannot get to the infectious disease specialist
44	There is no integration of medical services with community-run services	Consideration should be given to the widespread adoption of a hybrid model of care, where community representatives indicate facility-based services and redirect clients to external services if necessary

Thus, **the most significant gaps identified are:**

- Long chain from testing to treatment, due to limitations while testing and conducting epidemiological studies;
- No recommendation for the use of DTG and EFV400 in first-line regimens, both preferred and alternative;
- Lack of regulation on the use of PEP and PrEP;
- the importance of comprehensive care and involvement of patient communities in service delivery is not defined.

In general, the national clinical protocol (the CP HIV 2017) complies with the 2016 WHO Guidelines but taking into account the development of WHO recommendations in the period 2017-2019 and considering a number of identified discrepancies and gaps in regulation, it should be recommended for the national health authorities of Belarus harmonizing national protocols, bringing them in line with the current WHO guidelines on the above-mentioned points.

Bosnia and Herzegovina

List of documents:

- Protocol name, year: Clinical Guidelines for HIV and AIDS Treatment, Sarajevo, 2016.
- Protocol name, year: HIV Counseling and Testing, Sarajevo, 2016.
- UNAIDS and Country Coordinating Mechanism: Transition for the Continuation of HIV and AIDS Prevention, Treatment and Care in Bosnia and Herzegovina 2015-2017
- Response to HIV/AIDS in Bosnia and Herzegovina (Council of Ministers of B&H – Strategy 2011-2016)

Part 1. Basic information	
Name of the current version of document and the and a link to it.	Clinical Guidelines for HIV/AIDS Treatment, Sarajevo, 2016. Protocol: HIV Counseling and Testing, Sarajevo, 2016 UNAIDS and Country Coordinating Mechanism: Transition for the Continuation of HIV and AIDS Prevention, Treatment and Care in Bosnia and Herzegovina 2015-2017
Year of the current version.	2016
No. of the normative document defining the status of these recommendations (order, resolution, if applicable).	Response to HIV/AIDS in Bosnia and Herzegovina (Council of Ministers of B&H – Strategy 2011-2016)
Legal status of recommendations: mandatory or advisory in nature, what additional documents govern the need for recommendations.	Recommended - advisory
Frequency of the document revision (is it defined? by which documents is it regulated?).	Every 3-4 years. Next revision and updates of the Guidelines and the Protocol is expected by the beginning of 2020
Level of evidence (description of the applicable system).	N/A
Members of the editorial board (are representatives of NGOs/patient organizations included?).	Members of the Board: Ministry of Health Federation of Bosnia and Herzegovina; Ministry of Health of the Republic of Srpska; UNDP; Global Fund; 2 NGOs (Partnership for Health and SIDA)
List and brief description of documents additionally regulating the use of ARVs in the country, including the following documents, but not limited to: · laws governing the nature of supplying the ARVs (free of charge/ paid, by prepaid medical care plan or at the expense of a special national program, etc.); · lists of Vital and Essential Drugs; · lists of drugs to be procured at the expense of different budgets; · treatment standards, etc.	Official Gazette: a) ARV drugs are free of charge for population covered by any health and social insurance. Expenses for ARVs, treatment and care are paid by national program: The Solidarity Fund of F B&H. b) Essential ARV drugs available in B&H: ZDV, ddI, d4T, 3TC, ABC, ZDV+3TC, NVP, EFV, LPV/r, IDV, RTV, NFV, SQV, TDF, TDF+FTC, ABC+3TC, RAL c) No different budgets for these drugs d) N/A

Page and quote from national protocols	**Comment**
Part 2. Guidelines for diagnostics	
Retesting before inclusion in care and treatment programs.	Before inclusion in care and treatment program, testing of CD4 and VL is obligatory as well as confirmatory testing, afterwards ART can be initiated
Pre-test and post-test advising services.	In the Clinic for Voluntary Confidential Counseling and Testing (VCCT) is performed; counseling before and after testing is mandatory. Protocol: HIV Counseling and Testing, Sarajevo, 2016, page 15 and 35

Testing by non-professional medical workers using express diagnostic methods.	Testing and counseling is exclusively entrusted to experienced medical professionals
Testing initiated by a medical worker.	Testing is offered to clients presenting with HIV Indicator Conditions and Diseases
Diagnosis of HIV infection in children and infants, in particular, the sensitivity and specificity of tests.	PCR HIV RNA in first 48 hours after birth, afterwards 6 weeks after labor, 3 and 6 months after childbirth; at the age of 18 months ELISA testing of infant. Clinical Guidelines for HIV/AIDS Treatment, Sarajevo, 2016, page 56-59
Testing in special groups (adolescents, pregnant women, couples and partners).	**Adolescents:** testing is allowed without permission of foster parents for those 15 years of age or older. **Pregnant women:** testing is offered (not mandatory). **Couples and partners:** are encouraged to have counseling and testing together. (Protocol: HIV Counseling and Testing, Sarajevo, 2016., page 28-33)
Diagnostic algorithms.	Two screening tests of two different manufacturers; if positive testing, confirmatory HIV testing is performed using Western blot. In case of indeterminate WB results, HIV RNA PCR is performed. (Protocol: HIV Counseling and Testing, Sarajevo, 2016., page 33-34)
Part 3. ARVs for HIV prevention	
Pre-exposure prophylaxis of HIV infection.	PrEP is available since 2016 in B&H. PrEP is used for MSM only. Before starting PrEP, testing on HIV and STI is performed. In case of negative results of testing, the following PrEP is prescribed: TDF/FTC 300/200mg, 2 tablets, 2-24 hours before sexual intercourse, Followed by 2 single doses of TDF/FTC, 24 and 48 hours after the first drug intake. Clinical Guidelines for HIV/AIDS Treatment, Sarajevo, 2016, page 50-51
Algorithm and regimens of post-exposure prophylaxis for different population groups, including for PMTCT.	PEP: for HIV occupational and non-occupational exposure, as well as for cases of sexual assault. **Evaluation of source of possible HIV infection:** (HBsAg, anti-HCV, anti-HIV; if the source is a HIV-positive person on ART, then testing of resistance is performed in case of detectible VL. **Evaluation of exposed person:** HBV, HCV, HIV serostatus, pregnancy testing (in case of negative results, contraception is prescribed). **HIV PEP prescribing:** TDF/FTC (or ZDV/3TC) + LPV/r (or RAL). HBV immunoprophylaxis. HCV serologic monitoring. · Clinical follow-up. · Clinical Guidelines for HIV/AIDS Treatment, Sarajevo, 2016, page 48-49
Part 4. Antiretroviral therapy regimens	
When ART should be started, including recommendations for specific groups of patients (for whom urgent indication is recommended).	ART is initiated as soon as HIV infection is diagnosed, regardless of CD4 counts, nevertheless from which specific group the patient is. Clinical Guidelines for HIV/AIDS Treatment, Sarajevo, 2016, page 39
Choosing the Line 1 drugs, including: · Preferences for fixed dose combination (FDCs) drugs. · Refusal to use stavudine. · Use of DTG and EFV400 in accordance with the updated recommendations (2018, 2019). · Recommendations for use of dolutegravir in women of childbearing age and pregnant women.	EFV + TDF/FTC or ABC/3TC; or LPV/r + TDF/FTC or ABC/3TC; or RAL + TDF/FTC or ABC/3TC - Preferred fixed combination: TDF/FTC - Stavudine is not in use anymore in B&H Notes: - DTG and EFV 400 are not available in B&H - DTG will be available by the beginning of 2020.
Line 1 ART for special patient groups.	PMTCT: ZDV + 3TC + LPV/r Clinical Guidelines for HIV/AIDS Treatment, Sarajevo, 2016, page 80
Recommendations for breastfeeding of babies.	HIV-positive mothers are advised to avoid breastfeeding

Monitoring before and after starting ART.	CD4 monitoring before starting ART, afterwards every 3-6 months during the first 2 years after starting ART, or if CD4<300 cells/uL. VL before starting ART, 4 weeks after starting treatment, afterwards every 8 weeks until VL becomes suppressed, then every 3-4 months until the patient is stable (for stable suppressed patients every 6 months) Clinical Guidelines for HIV/AIDS Treatment, Sarajevo, 2016, page 14-15
Recommendations for switching to Line 2 ART regimens, including for special patient groups, including the preferred alternative regimen.	EFV + ZDV/3TC or TDF/3TC; LPV/r + ZDV/3TC or TDF/3TC NVP + ZDV/3TC or TDF/3TC
Recommendations for Line 3 ARVs.	
Barriers to accessing key drugs recommended by WHO, when they are available (e.g., no registration, no inclusion in the list of Vital and Essential Drugs or procurement lists, high price, etc.)	Barriers in B&H: Only registered drugs are available from the List of drugs of the Solidarity Fund of B&H. Registration of new ARV drugs and inclusion in the List of Essential drugs is rather complicated. Prices of ARV drugs are high, since some important pharmaceutical companies are not present (B&H is a small market with low HIV incidence and limited number of patients) N/A
Part 5. Prevention and treatment of co-infections and co-morbidities	
Recommendations for the prevention and treatment of co-infections, primarily (but not limited to): · HIV/HCV · HIV/HBV · HIV/TB	All HIV-positive persons are tested for HBV and HCV, screening for TB. · HIV/ HCV: DAA + ART · HIV/HBV: immunization for HBV. First-line ART: TDF + FTC (or 3TC) + EFV · HIV/TB: Isoniazid preventive therapy. Treatment: DOTS Clinical Guidelines for HIV/AIDS Treatment, Sarajevo, 2016, page 121-140
Prevention and treatment of relevant noncommunicable diseases: · Cardiovascular diseases · Depression · Diseases of the central nervous system · Kidney diseases · Substance use	· Cardiovascular diseases: regulation of body mass index, smoking cessation, regulating lipid abnormalities, avoiding use of IP and ABC because of CVD risk · Depression: screening of depression in family history; elderly patients, adolescents; use of EFV, neurotropic and recreational drugs. · Kidney diseases: testing proteinuria; regulation of hypertension; nephrotoxic drugs (including ART drugs); renal ultrasound, eGFR · Substance abuse: Screening on drug use; Interaction of ART and psychoactive compounds; Exchange of needles and syringes program; Opioid substitution therapy Clinical Guidelines for HIV/AIDS Treatment, Sarajevo, 2016, page 86
Part 6. Provision of health services	
The provision of health services, including but not limited to: · Recommendations for decentralization of services. · Recommendations for redistribution and delegation of services. · Recommendations for integration of services.	Decentralized system of provision of health services. In B&H, there are three clinics for HIV treatment and care: Sarajevo, Tuzla and Banja Luka. In B&H there are 12 VCCT centers (Voluntary Confidential Counseling and Testing).
Part 7. Other clinically significant discrepancies that do not fall within the thematic blocks above	
Other clinically significant discrepancies that the experts are aware of, between the WHO recommendations for the diagnosis and use of antiretroviral drugs and national recommendations, for example, in the part of providing harm reduction services for patients who use psychoactive substances, etc.	No major discrepancies with WHO recommendations and B&H national recommendations and guidelines

Georgia

List of documents:

- Protocol name, year: Consolidated guidelines on the use of antiretroviral drugs for the prevention and treatment of HIV/AIDS, 2018

Part 1. Basic information	
Name of the current version of document and the and a link to it.	Consolidated guidelines on the use of antiretroviral drugs for the prevention and treatment of HIV/AIDS
Year of the current version.	2018
No. of the normative document defining the status of these recommendations (order, resolution, if applicable).	Decree №01-158 of 5 July 2018 of the Minister of Labour, Health and Social Affairs of Georgia
Legal status of recommendations: mandatory or advisory in nature, what additional documents govern the need for recommendations.	As elsewhere in civilized world national clinical practice guidelines in Georgia is a set of recommendations that define the standard of care for HIV. No specific status (mandatory or obligatory) are assigned to guidelines, but deviation from guideline recommendations may result in specific inquiry. As defined in the Ministerial decree N94/n of 27 Match 2006 on developing national clinical practice guidelines – the guideline is the recommendation for the clinical management of specific conditions following the principles of evidence-based medicine, which is the document representing national health policy and which is approved by the Minister of Labour Health and Social Affairs. The guidelines represent the basis for national HIV treatment program, including procurement of ARVs in accordance with guideline recommendations.
Frequency of the document revision (is it defined? by which documents is it regulated?)	The national manual for developing clinical practice guidelines recommends to conduct revision at least in 3 year or earlier if new evidence emerges. Revision of current version is planned to be completed in 2020
Level of evidence (description of the applicable system).	The national guidelines represents adaption of internationally recognized guidelines, which is primarily based on 2016 WHO document, specific aspects not covered by WHO were incorporated from EACS guidelines 9.0 and US DHHS guidelines on pediatric HIV. Therefore, independent synthesis of evidence was not conducted, but rather relied on methodology used in the above referenced international documents.
Members of the editorial board (are representatives of NGOs/patient organizations included?).	Current version of guidelines was developed by panel of 8 experts that included clinicians, health systems expert, public health expert, laboratory expert and a community representative
List and brief description of documents additionally regulating the use of ARVs in the country, including the following documents, but not limited to: · laws governing the nature of supplying the ARVs (free of charge/ paid, by prepaid medical care plan or at the expense of a special national program, etc.); · lists of Vital and Essential Drugs; · lists of drugs to be procured at the expense of different budgets; · treatment standards, etc.	The national clinical practice guidelines on HIV provides sufficient detail on standards of clinical management of HIV, including clinical assessments, laboratory examinations and ART prescription. Operational issues related to HIV clinical care delivery, including budgetary issues are defined in the national strategic plan and national HIV program. The program is annually renewed, the program for 2020 was approved by the decree of the Government of Georgia #674 of 31 December 2020. The national program on HIV/AIDS provides funding for healthcare based HIV testing services, PrEP, PEP, outpatient and inpatients services, including ART. The national program defines that all citizens of Georgia and certain groups of non-citizens living in the country are entitled to receive free HIV clinical care including ARVs and HIV related examinations. 2020 national program covers 100% of first line ART drugs and 80% of second/third line regimens. The Global Fund supports civil society based HIV testing services for key populations, 20% of second/third line ARV costs as well as prevention activities.
Other relevant information	2018 version of guidelines represents revision of 2017 version. This was partial revision affected selection of first line ART regimens in adults, otherwise the guideline remained the same primarily following recommendation from 2016 WHO consolidated guidelines. Georgia national guidelines adapted the following chapters from WHO guidelines: · ARVs for HIV prevention · ART · Managing common coinfections and comorbidities Chapters on 'HIV diagnosis' and "Service delivery" are not incorporated in guidelines. Issues related to HIV diagnosis are governed by national guidelines on HIV surveillance, service delivery – by national HIV program.

Page and quote from national protocols	Comment	Link to relevant WHO recommendation, page, document, quote
Part 2. Guidelines for diagnostics		
Retesting before inclusion in care and treatment programs.	As part of initial assessment, all newly diagnosed patients entering HIV care are tested for HIV viral load (National ART guidelines, Table 5, page 28) Recommendation to measure plasma HIV RNA at entry into care has been adopted from EACS guidelines. Although the primary reason for this recommendation is to set the baseline value for measuring response to treatment in first several months of ART initiation, this approach meets WHO recommendation for verifying the diagnosis.	**2016 WHO guidelines:** chapter 2.2 Retesting prior to enrolment in care, page 19 · National programmes should retest all people newly and previously diagnosed with HIV before they enrol in care and initiate ART. · Retesting people on ART is not recommended, as there are potential risks of incorrect diagnosis, particularly for in vitro diagnostics (IVDs) that use oral fluid specimens.
Pre-test and post-test advising services.	According to national HIV surveillance guidelines post-test advise in mandatory for all patients testing positive for HIV. Pre-test is not required for blood donors (mandatory testing) and pregnant women (pot-out testing). All other populations, including those tested through community- or facility-based approaches, should receive pre- and post-test counseling. The counseling procedure is detailed in surveillance guidelines, which should be conducted following principles of voluntarity, confidentiality and protection of human rights. The guidelines instruct how to counsel, what type of information should be collected and how to link persons to appropriate services.	2016 WHO guidelines: chapter 2.3 Pre- and post-test services, page 20
Testing by non-professional medical workers using express diagnostic methods.	There are no regulations prohibiting lay professionals to conduct HIV testing	**2016 WHO guidelines:** 2.4 Principles of and approaches to service delivery, page 24 Lay providers who are trained and supervised can independently conduct safe and effective HIV testing using rapid diagnostic tests
Testing initiated by a medical worker.	According to national HIV surveillance guidelines medical worker can initiate HIV testing if patient reports high risk behavior or has HIV indicator condition, including TB	**2016 WHO guidelines:** 2.4.2 HIV testing service approaches, page 26. PITC should be offered for clients (adults, adolescents and children) in clinical settings who present with symptoms or medical conditions that could indicate HIV infection, including presumed and confirmed TB cases.
Diagnosis of HIV infection in children and infants, in particular, the sensitivity and specificity of tests.	According to national HIV surveillance guidelines HIV diagnosis in infant relies on repeated nucleic acid based testing performed at birth and preferably repeated within 4 weeks of life. Antibody testing is not recommended until the age of 18 months Guidelines do not define sensitivity and specificity threshold	**2016 WHO guidelines:** 2.5 HIV diagnosis in infants and children, page 28 Addition of nucleic acid testing (NAT) at birth to existing early infant diagnosis (EID) testing approaches can be considered to identify HIV infection in HIV-exposed infants
Testing in special groups (adolescents, pregnant women, couples and partners).	National surveillance guidelines define the following populations as a focus of surveillance system: · Key populations (PWiD, MSM, FSW, Prisoners) and their partners · Partners of HIV positive persons · Pregnant women · Infants born to HIV+ mothers · Patients with TB · Patients with STIs · Patients with hepatitis B and C · Patients with any other HIV indicator conditions not listed above · These populations include persons of all genders and age.	**2016 WHO guidelines:** 2.6 Other priority populations, page 42 Adolescents Pregnant women Couples and partners Men Key populations
Diagnostic algorithms.	According to national HIV surveillance guidelines in persons aged 18 month and older HIV diagnosis is relied on antibody test – screening test (rapid or ELISA test) followed by confirmatory testing (Western Blot or in special circumstance NAT)	

Part 3. ARVs for HIV prevention		
Pre-exposure prophylaxis of HIV infection.	Recommendations on PrEP is provided in the chapter 3 entitled "Pre-exposure prophylaxis" page 19, quote: "Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches. The PrEp regimen is tenofovir/emtricitabine (300/200 mg), one tablet a day. Duration of PrEP should be tailored individually."	**2016 WHO guidelines, chapter 3.1, page 52. Quote:** "Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches"
Algorithm and regimens of post-exposure prophylaxis for different population groups, including for PMTCT.	Chapter 4, page 22: **Adults and adolescents:** · TDF + 3TC (or FTC) should be used as preferred backbone · LPV/r or ATV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for adults and adolescents (conditional recommendation, very low-quality evidence). Where available, RAL, DRV/r, or EFV can be considered as alternative options. **Children:** · AZT + 3TC is recommended as the preferred backbone regimen · LPV/r is recommended as the preferred third drug. An age-appropriate alternative regimen can be identified among ATV/r, RAL, DRV, EFV and NVP.	**2016 WHO, chapter 3.2, page 62:** **Adults and adolescents:** · TDF + 3TC (or FTC) is recommended as the preferred backbone regimen · LPV/r or ATV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for adults and adolescents (conditional recommendation, very low-quality evidence). Where available, RAL, DRV/r, or EFV can be considered as alternative options. **Children:** · AZT + 3TC is recommended as the preferred backbone regimen · LPV/r is recommended as the preferred third drug. An age-appropriate alternative regimen can be identified among ATV/r, RAL, DRV, EFV and NVP.
Other points not mentioned above.	National HIV program for 2020 (decree of the Government of Georgia #674 of 31 December 2020) is designed in accordance with 2018 WHO interim guidelines on PEP and the current version of the national program recommends DTG as preferred third drug for post-exposure prophylaxis. This will be reflected in 2020 revision of national guidelines	**2018 WHO Interim guidelines, chapter 4, page 37:** - DTG is recommended as the preferred third drug for HIV post-exposure prophylaxis
Part 4. Antiretroviral therapy regimens		
When ART should be started, including recommendations for specific groups of patients (for whom urgent indication is recommended).	**National guidelines** **Adults (chapter 6.1, page 35):** · ART should be initiated in all adults living with HIV, regardless of clinical stage and at any CD4 cell count **Pregnant and breastfeeding women (chapter 6.1, page 35):** · ART should be initiated in all pregnant and breastfeeding women living with HIV regardless of clinical stage and at any CD4 cell count and continued lifelong **Adolescents (chapter 6.1, page 35):** · ART should be initiated in all adolescents living with HIV, regardless of clinical stage and at any CD4 cell count **Infants and children (<10 years) (chapter 6.1, page 35):** · ART should be initiated in all children living with HIV, regardless of clinical stage or at any CD4 cell count	**2016 WHO guidelines** **Adults (chapter 4.3.1, page 74):** · ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count **Pregnant and breastfeeding women (chapter 4.3.2, page 81):** · ART should be initiated in all pregnant and breastfeeding women living with HIV regardless of WHO clinical stage and at any CD4 cell count and continued lifelong **Adolescents (chapter 4.3.3, page 86):** · ART should be initiated in all adolescents living with HIV, regardless of WHO clinical stage and at any CD4 cell count **Infants and children (<10 years) (chapter 4.3.4, page 89):** · ART should be initiated in all children living with HIV, regardless of WHO clinical stage or at any CD4 cell count

	Timing of ART for adults and children with TB (chapter 6.1.1, page 36) • ART should be started in all TB patients living with HIV, regardless of CD4 cell count • TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment • HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm3) should receive ART within the first two weeks of initiating TB treatment.	**Timing of ART for adults and children with TB (chapter 4.3.5, page 93)** • ART should be started in all TB patients living with HIV, regardless of CD4 cell count • TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment • HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm3) should receive ART within the first two weeks of initiating TB treatment.
Choosing the Line 1 drugs, including: • Preferences for fixed dose combination (FDCs) drugs. • Refusal to use stavudine. • Use of DTG and EFV400 in accordance with the updated recommendations (2018, 2019). • Recommendations for use of dolutegravir in women of childbearing age and pregnant women.	National guideline does not provide specific recommendation about FDCs, this and other service delivery aspects are defined in the national HIV program. 2020 procurement of ARVs includes delivery of TDF/3TC/DTG and TDF/FTC/EFV FDCs. Stavudine in Georgia was phased out after 2007 revision of national guidelines and has not been in use for at least 11 years **1st line regimens (Chapter 6.2, page 41):** **Adults:** Preferred: TDF+3TC(FTC)+DTG Alternative: a) ABC+3TC+DTG; b) TDF+3TC(FTC)+EFV; c) ABC+3TC+EFV; d) TDF + 3TC(FTC) + NVP. Special circumstances: Boosted PI containing regimens Notes: ABC can only be prescribed based on HLA B*5701 testing; EFV in adults can be prescribed as 600 or 400 mg formulation **Adolescents:** Preferred: TDF+3TC(FTC)+EFV Alternative: a) AZT + 3TC + EFV (or NVP); b) TDF + 3TC (FTC) + DTG; c) TDF + 3TC (FTC) + EFV400 d) TDF + 3TC (FTC) + NVP Special circumstances: ABC and boosted PI containing regimens **Children (3-10 years):** Preferred: ABC + 3TC + EFV Alternative: a) ABC + 3TC + NVP b) AZT + 3TC + EFV (NVP); c) TDF + 3TC (FTC) + EFV (NVP) Special circumstances: boosted PI containing regimens **Children (<3 years):** Preferred: ABC (or AZT) + 3TC + LPV/r Alternative: ABC (or AZT) + 3TC + NVP **Pregnant/breastfeeding women:** Preferred: TDF+3TC(FTC)+EFV Alternative: a) AZT + 3TC + EFV (NVP); b) TDF + 3TC (or FTC) + NVP Special circumstances: ABC and boosted PI containing regimens NOTE: National EMTCT guidelines issued in 2019, which is current standard of care define the use of DTG in pregnant women. According to these guidelines a) DTG should not be prescribed to pregnant women during the first trimester of pregnancy; b) DTG can be prescribed after the first trimester of pregnancy; c) if women is already on DTG the drug should be continued. (National EMTC guidelines, approved by ministerial decree N 01-444)	**2019 WHO updated recommendations** **1st line regimens (Table 1, page 7):** **Adults and adolescents, including pregnant** **Preferred:** TDF+3TC(FTC)+DTG Alternative: TDF+3TC(FTC)+EFV400 Special circumstances: TDF + 3TC (or FTC) + EFV 600 AZT + 3TC + EFV 600 TDF + 3TC (or FTC) + PI/r TDF + 3TC (or FTC) + RAL TAFc + 3TC (or FTC) + DTG ABC + 3TC + DTG **Children** Preferred: ABC+3TC+DTG Alternative: ABC + 3TC + LPV/r ABC + 3TC + RAL TAF + 3TC (or FTC) + DTG Special circumstances: ABC + 3TC + EFV (or NVP) AZT + 3TC + EFVg (or NVP) AZT + 3TC + LPV/r (or RAL) **Neonates:** Preferred: AZT+3TC+RAL Alternative: AZT + 3TC + NVP Special circumstances: AZT + 3TC + LPV/r
Line 1 ART for special patient groups.	TDF+3TC(FTC)+EFV for TB/HIV, if EFV could not be prescribed double dose DTG is an alternative option All patients with HIV/HBV co-infection should receive TDF/FTC backbone	

Recommendations for breastfeeding of babies.	National ART guidelines do not provide any specific recommendation on breastfeeding. The choice of breastfeeding or artificial feeding is mother's informed decision after thorough discussion with clinician. National EMTCT guideline recommends avoiding breastfeeding in mothers with viral load >50 copies/ml	**2016 WHO guidelines: Chapter 4.4.8, page 125** **Recommendations** National or subnational health authorities should decide whether health services will principally counsel and support mothers known to be HIV infected to either breastfeed and receive ARVa interventions or avoid all breastfeeding. In settings where national authorities have decided that maternal and child health services will principally promote and support breastfeeding and antiretroviral interventions as the strategy that will most likely give infants born to mothers known to be HIV infected the greatest chance of HIV-free survival, mothers known to be infected with HIV should exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life.b Breastfeeding should then stop only once a nutritionally adequate and safe diet without breast milk can be provided (strong recommendation, high-quality evidence for the first 6 months; low-quality evidence for the recommendation of 12 months).
Monitoring before and after starting ART.	**HIV diagnosis (Chapters 5.1-5.5, page 23-33)** clinical examination, CD4 count, viral load, CBC, screening for TB and other opportunistic infections, viral hepatitis serology, liver function tests, kidney function tests, assessment of NCDs, instrumental examinations, as necessary. Additional assays are performed, as necessary. **Follow-up before ART (if not initiated) (chapter 5.6, page 34):** CD4 every 6 months, viral load every 12 months, CBC and clinical chemistry assays, instrumental examinations, as necessary. Additional assays are performed, as necessary. **On ART (chapter 6, page 63):** Viral load, CD4 cell count, CBC, liver and kidney function tests every 6 months, HIV drug resistance testing if virologic failure documented. Adherence monitoring. ARV toxicity monitoring, TB, OI and NCD assessment. Additional assays are performed, as necessary.	**2016 WHO guidelines (Table 4.10, page 128)**
Recommendations for switching to Line 2 ART regimens, including for special patient groups, including the preferred alternative regimen.	Switch to 2nd line is indicated if virologic failure is documented defined as two consecutive viral load measurements of >50 copies/ml in patients on ART for at least 6 months period. Patients with virologic failure should undergo HIV drug resistance testing (Chapter 6.4.2, page 65). Selection of 2nd line regimen should be based on HIV drug resistance test (chapter 6.5.1, page 74-75). Drugs for second line regimen should be selected based on drug resistance mutation panel from available drug classes: NRTI, PI, INSTI. LPV/r and ATVr are preferred PI options for the first second line treatment, while DRV is reserved for more treatment experienced patients. DTG is preferred INSTI, while RAL is reserved for more treatment experienced patients. If HIV drug resistance testing could not be performed, treatment switch is guided by previous treatment experience in accordance with 2016 WHO treatment switch guidelines (Table 23 of national guidelines, page 76).	**2016 WHO Guidelines (page 129):** Viral failure is defined by a persistently detectable viral load exceeding 1000 copies/mL (that is, two consecutive viral load measurements within a 3-month interval with adherence support between measurements) after at least 6 months of starting a new ART regimen. **2016 WHO guidelines:** Table 4.15. Preferred second-line ART regimens for adults, adolescents, pregnant women and children page 150. **2019 WHO Updated recommendations:** Table 2. Preferred and alternative second-line ART regimens, page 8.
Recommendations for Line 3 ARVs.	Similar definition of virologic failure and treatment selection strategies are applied for 2nd and 3rd line treatments. Selection of 3rd line regimen is guided by HIV drug resistance testing from active drugs. DRV/r, RAL and ETV are reserved for 3rd line treatment. If HIV drug resistance testing could not be performed, treatment switch is guided by previous treatment experience in accordance with 2016 WHO treatment switch guidelines (Table 24 of national guidelines, page 77).	**2016 WHO guidelines:** Table 4.19. Summary of sequencing options for first-, second- and third-line ART regimens in adults, adolescents, pregnant women and children page 161.

Barriers to accessing key drugs recommended by WHO, when they are available (e.g., no registration, no inclusion in the list of Vital and Essential Drugs or procurement lists, high price, etc.)	No barriers to accessing drugs recommended by WHO have ever been documented	N/A
Part 5. Prevention and treatment of co-infections and co-diseases		
Recommendations for the prevention and treatment of co-infections, primarily (but not limited to): · HIV/Viral Hepatitis C (HCV) · HIV/HBV · HIV/TB	**HIV/HCV:** All patients entering HIV care are screened for HCV antibodies, if negative serologic testing is repeated annually. HCV RNA PCR can be performed as initial test if acute//recent HCV infection is suspected. Patients positive for anti-HCV are tested for HCV RNA using PCR (Table 5, page 29; Table 20, page 60). Patients with chronic HCV infection are managed/treated in accordance with national hepatitis C elimination program treatment protocols first developed in 20 April 2015 and last updated 31 December 2019 (Decree of Government of Georgia N 677) **HIV/HBV:** All patients entering HIV care are screened for HBV serologic markers – HbsAg and HBs antibodies. Patients negative for all markers are offered free HBC vaccine within the national HIV program. Response to vaccination is measured by quantifying antibody titers. Patients positive for HBsAg are screened for HDV, HBV DNA or if not possible for HBeAg (Table 5, page 29; Chapter 5.5, page 33; Table 20, page 60). HIV/HBV patients are started don TDF/3TC(FTC) containing regimen. **TB/HIV:** TB symptom screening is recommended at the time of entry into HIV care and thereafter at each clinical visit. Patients with symptoms of TB should be screened for active diseases using Xpert MTB/RIF (Table 5, page 29). Preventive treatment with isoniazid is recommended for all patients after excluding active TB (chapter 5.5, page 33). Detailed recommendation on the prevention and management of TB/HIV co-infections are provided in the national TB/HIV protocol of the national TB management guidelines.	**2016 WHO Guidelines:** 5.2.4 Hepatitis B and C, page 208 5.2.2 Tuberculosis, page 196
Prevention and treatment of relevant noncommunicable diseases: · Cardiovascular diseases · Depression · Diseases of the central nervous system · Kidney diseases · Substance use	Prevention and management of NCDs is recommended as an essential package of services. Specific recommendations include assessment at the entry into HIV care and continuous monitoring in accordance with standard protocols developed for general population. This includes: · blood pressure measurement, lipid profile, and Framingham risk score for cardiovascular diseases · Serum creatinine, urine analysis and eGFR to monitor kidney function · Fasting glucose for monitoring diabetes · Bone health monitoring through measuring vitamin D and performing densitometry as indicated · Cancer screening including mammography, pap smear, ultrasound for patients with liver cirrhosis · Assessment of cognitive function and depression using standardized tools (Table 5, page 29; Table 6, page 30, Chapter 6.4.6 page 74) Information of substance abuse, including on OST, is recommended to collect at the entry into HIV care (Table 5.1, page 23), opioid substitution therapy is identified as one of the options for adherence support (Chapter 6.3, page 58)	**2016 WHO guidelines:** Chapter 5.3 Prevention, screening and management of other comorbidities and chronic care for people living with HIV, page 215.
Part 6. Provision of health services		
The provision of health services	Not applicable	

Analytical summary

Overall Georgian treatment guidelines follow the WHO guidance related to HIV diagnosis and use of ARVs for the treatment and prevention of HIV infection. Although the pace WHO is updating its recommendations makes it difficult to reflect changes in the guidelines, latest WHO recommendations have been incorporated in practice through changes in the national HIV program. Even though new WHO recommendations have been implemented in real-life practice, these need to be documented in updated guidelines. The guidelines panel has been working on update and the new version is expected to be approved in 2020.

HIV Diagnosis:

Georgia's recommendations on HIV testing and diagnosis follows the best international practices, including WHO recommendations. Facility- and community-based testing, including through rapid diagnostic tests, is widely available, nucleic acid based testing is routinely used for early infant diagnosis, current recommendations cover all populations that determine epidemic trajectories in the country.

Few discrepancies have been identified:

National guidelines do not identify adolescents as separate population as all recommendations apply to all age categories. Secondly, epidemiological data indicates that adolescents in Georgia do not meet the definition of affected population and account for only small proportion of PLHIV. Decision to identify adolescents as separate target population should be based on the epidemiological evidence.

No specific recommendation on HIV testing delivery by lay providers is formulated in guidelines. AT the same time there are no regulation prohibiting lay providers to deliver HIV testing services and they are engaged in service delivery. Nevertheless, incorporating WHO's recommendation on this would be helpful to further promote uptake of HIV testing through community-based services, including outreach.

Georgian national guidelines do not specify sensitivity and specificity requirements for diagnostics tests. We believe that this recommendation goes beyond powers of clinical practice guidelines as defined by national regulations. Sensitivity and specificity of diagnostics tests are operational issue that needs to be addressed by the national program and procurement regulations. Only high-quality diagnostic tests, based on FDA approval, CE marking or WHO prequalification, are procured in Georgia including antibody and NAT tests.

ARVs for HIV prevention:

Georgia's PrEP recommendations fully follow 2016 WHO guidelines and further to this provide clear instructions about the medical management of PrEP clients. Similar to WHO guidelines, the national guidelines recommend continuous PrEP approach, while sufficient evidence accumulated since its approval that intermittent (on-demand) PrEP is also highly effective and thus this needs to be reflected in national guidelines.

The current version of Georgian national guidelines have been approved on July 3, 2018 and therefore selection of PEP regimen relied on 2016 WHO guidance recommending TDF + 3TC (FTC) in combination with LPV/r or ATV/r. Later in 2018 WHO updated its guidelines to recommend DTG as preferred third option resulting in discrepancy between currently approved national and latest WHO guidelines. Following this update, Georgian national HIV program for 2020 was designed to recommend DTG as preferred third drug. This change implemented in practice needs to be formalized in new revision of guidelines to be completed in 2020.

Antiretroviral therapy regimens

ART initiation criteria fully comply with WHO recommendations, in fact Georgia implemented "treat all" policy already in 2015

The regimen of TDF+3TC(FTC)+DTG was defined as preferred first line option in adults even earlier than official WHO recommendations were issued in December 2018. Selection of alternative regimens are similar with few minor differences – WHO prioritizing EFV400mg while national guidelines recommends using both 400 and 600mg formulations. Also, Georgian guidelines kept NVP as 4th alternative option if neither DTG nor EFV can be prescribed, while WHO included RAL for special circumstances.

Selection of 1st line ART for adolescents in Georgian guidelines remained same as 2016 WHO recommendations, primarily due to the lack of evidence on DTG use in this population at the time of guidelines revision. Along with other new recommendations this has been considered in national HIV program and will be formalized in 2020 update of guidelines.

At the end of 2019, a total of 950 HIV-infected adults and adolescents ≥10 years old were on DTG-containing treatment representing 23% of all people on first line ART. According to national HIV program the proportion of people receiving DTG-containing regimens will increase to up to 50% by the end of 2020.

Selection of 2nd and 3rd line regimens relies on HIV drugs resistance testing, which is routinely available since 2005. This ensures selection of most appropriate and potent regimen and avoids unnecessary switches. Regimen is selected from available drug classes, prioritizing ATV/r or LPV/r as first choice PI, and DTG over RAL. In rare cases when HIV drug resistance test result is not available treatment national guidelines recommend switching empirically in accordance with 2016 WHO guidelines, which needs to be updated in line with 2019 WHO recommendations,

At the end of 2019, a total of 197 patients were on DTG based second line ART, representing 24.6% of all people on 2nd line ART. 62 patients on 3rd line therapy, including combinations of PI/r + INSTI (either DTG or RAL), 4 patients receive Etravirine containing regimens.

Prevention and treatment of co-infections and co-diseases

National guidelines comprehensively cover management of co-infections and co-morbidities exceeding standards suggested by WHO.

Provision of health services

This chapter is not incorporated in the national guidelines, as it goes beyond requirements set for clinical practice guidelines. Issues related to service delivery are covered in national strategic plan and national HIV program.

Kazakhstan

Part 1. Basic information	
Name of the current version of the document and the link to it.	Clinical protocol for the diagnosis and treatment of HIV infection in adults
Year of the current version.	2017
The normative document number and its status (order, resolution, if applicable).	Approved by the Joint Commission on the Quality of Medical Services of the Ministry of Health of the Republic of Kazakhstan on May 12, 2017, Protocol No. 22
Legal status of recommendations: mandatory or advisory (What additional documents govern the need for recommendations).	Recommendatory nature, Code of the Republic of Kazakhstan dated September 18, 2009, No. 193-IV "About health of the people and health care system", paragraph 59-1 Regulation on the development/revision of clinical protocols
Frequency of the document revision (Is it defined? What documents regulate this?).	Revision of the protocol after 2 years; the frequency and conditions of protocol revisions are specified in the approved protocol itself
Level of evidence (description of the applicable system).	**Evidence level scale:** **A** High quality meta-analysis, a systematic review of RCTs, or large RCTs with very low likelihood (++) bias that can be generalized to the relevant population. **B** High quality (++) systematic review of cohort or case-control studies or high quality (++) cohort or case-control studies with very low risk of bias or RCTs with low (+) risk of bias that can be generalized to the relevant population. **C** A cohort or case-control study or controlled trial without randomization with a low risk of bias (+), the results of which can be generalized to the relevant population, or RCTs with a very low or low risk of bias (++ or +), the results of which cannot be directly extended to the relevant population. **D** Description of a series of cases or uncontrolled research or expert opinion. **GPP** Best Clinical Practice
Members of the editorial board (Are representatives of NGOs/patient organizations included?).	The team for the development of the current protocols included scientific and medical specialists, specialists in pharmacology and diagnostics, and health administrators. Before approval, the draft protocol is posted on the Open NLA portal for public discussion with the general population, associations, and non-governmental organizations. All individuals and legal entities within a month can leave their comments on the website or send their proposals for improving the document in the form of an official appeal.
List and a brief description of documents that additionally regulate the use of ARVs in the country, including the following documents, but not limited to: · Laws governing the nature of supplying the ARVs (free of charge/paid, by prepaid medical care plan or at the expense of a special national program, etc.); · Lists of vital and essential medicines; · Lists of medicines to be procured at the expense of different budgets; · Treatment standards, etc.	Order of the Minister of Health and Social Development of the Republic of Kazakhstan dated May 22, 2015 No. 369 "On approval of the Rules for the development and approval of the Kazakhstan national medicinal formulary" (the latest amendment by Order of the MoH of KR, No. ҚР DSM-70, dated May 8, 2019), regulates the Rules for the formation of the Kazakhstan national medicinal formulary, a list of medicines and medical devices for free and (or) preferential outpatient provision of certain categories of citizens with certain diseases (conditions), as well as the development of dosage forms for healthcare organizations. Order of the acting Minister of Health of the Republic of Kazakhstan, dated June 14, 2019, No. ҚР DSM-94, "On approval of the Rules for the implementation of the activities of the formulary system" regulates the rules for submitting an application for the assessment and selection of drugs in the Kazakhstan national drug formulary and the List of drugs and medical devices for free and (or) preferential outpatient provision of certain categories of citizens with certain diseases (conditions). Order of the Minister of Health of the Republic of Kazakhstan dated December 8, 2017 No. 931 "On approval of the Kazakhstan national medicinal formulary" (the latest amendments - Order of the Minister of Health of the Republic of Kazakhstan, dated April 25, 2019, No. ҚР DSM-51), regulates the list of medicines with proven clinical efficacy and safety, containing information on medicines and prices, which is an obligatory basis for the development of pharmaceutical forms for healthcare organizations and the formation of lists for the purchase of medicines within the guaranteed volume of free medical care and in the system of compulsory social health insurance Order of the Minister of Health of the Republic of Kazakhstan, dated January 31, 2018, No. 39 "On approval of the Rules for the formation of lists for the purchase of medicines and medical products within the guaranteed volume of free medical care and in the system of compulsory social health insurance." Order of the Minister of Health and Social Development of the Republic of Kazakhstan, dated September 30, 2015, No. 766 "On approval of the rules for providing citizens with medicines" (the latest amendments by the Order of the Minister of Health of the Republic of Kazakhstan, dated May 14, 2019, No. ҚР DSM-75). Determine the procedure for providing citizens with medicines in the Republic of Kazakhstan.

	Order of the Minister of Health of the Republic of Kazakhstan, dated August 29, 2017, No. 666. On approval of the List of medicines and medical devices within the guaranteed volume of free medical care, including certain categories of citizens with certain diseases (conditions), free and (or) subsidized medicines and medical devices at the outpatient level (latest amendments: order of the Minister of Health of the Republic of Kazakhstan dated May 14, 2019, No. ҚР DSM-76). Directive of the Government of the Republic of Kazakhstan, dated October 30, 2009, No. 1729 "On approval of the Rules for organizing and conducting the procurement of medicines, preventive (immunobiological, diagnostic, disinfecting) drugs, medical devices and medical equipment, pharmaceutical services for the provision of a guaranteed volume of free medical care and medical care in the system of compulsory social health insurance" (the latest amendments by Directive of the Government of the Republic of Kazakhstan, dated May 30, 2019, No. 347). Order of the Minister of Health of the Republic of Kazakhstan, dated July 18, 2018, No. 434 "On approval of the list of medicines, medical devices within the guaranteed volume of free medical care and in the system of compulsory social health insurance purchased from the Single Distributor for 2019" (last amendments by Order of the Minister Healthcare of the Republic of Kazakhstan, dated April 27, 2019, No. ҚР DSM-55).

Page and quote from national protocols	Comment	Link to relevant WHO recommendation, page, document, quote
Part 2. Diagnostic recommendations		
Retesting before inclusion in care and treatment programs.	There is no such recommendation in the national CP	**The 2016 WHO Guidelines, page 18:** National programs should retest all people newly and previously diagnosed with HIV before they enroll in care and initiate ART.
Pre-test and post-test consulting services	**Page 6, CP "HIV infection in adults":** during the initial visit, the patient is given psychosocial counseling about the positive HIV status. The patient signs a confidential interview sheet, form No. 264-7/u (the order of the MoH of RK, No. 907, dated November 23, 2010). Chapter 3 of the order of the MoH of RK, No. 246, dated 22 Apr. 2015 (the last amendment by the order of the MoH of RK, dated May 4, 2019, No. ҚР DSM-62) On approval of the Rules for voluntary anonymous and (or) confidential medical examination and counseling of citizens of the Republic of Kazakhstan, oral means, foreigners, and persons without citizenship permanently residing in the territory of the Republic of Kazakhstan, on HIV-infection issues free of charge.	**The 2016 WHO Guidelines, pages 19-24:** Pre-test information can be provided through group sessions, but everyone should be able to ask questions in confidence.
Testing by non-professional healthcare workers using express diagnostic methods.	**Page 8, CP "HIV infection in adults":** RT for HIV, followed by ELISA testing of key population groups (PWID, CSW, MSM) in trust points, friendly offices, NGOs. **Clause 4, Chapter 2 of the Order of the MoH of RK, No. 246, dated April 22, 2015** (the last amendment by the order of the MoH RK, dated May 4, 2019, No. ҚР DSM-62): Anonymous testing for HIV infection is conducted using rapid tests that detect antibodies to HIV-1, 2, and viral antigen p24. Anonymous HIV testing is conducted by healthcare organizations working in the field of HIV prevention and non-governmental organizations working with key populations.	**The 2016 WHO Guidelines, pages 25, 27:** Lay providers who are trained and supervised can independently conduct safe and effective HIV testing using rapid diagnostic tests (RDTs) (strong recommendation, moderate-quality evidence)...
Testing initiated by a healthcare worker.	Order of the Minister of Health and Social Development of the Republic of Kazakhstan dated June 23, 2015 No. 508 "On Approval of rules for mandatory confidential medical examination of people for HIV infection according to clinical and epidemiological indications," Section 2, "Procedure for conducting mandatory confidential medical examination of people for HIV infection according to clinical and epidemiological indications"	**The 2016 WHO Guidelines, page 26: Facility-based HIV testing services** Facility-based HIV testing services – often referred to as provider-initiated testing and counseling (PITC)... or by private medical practitioners. They may be offered in a range of clinical settings, depending on the type of epidemic, the population served, and the capacity of the facility.

Diagnosis of HIV infection in children and infants, in particular, the sensitivity and specificity of tests.	Pages 9-10, Clinical protocol for the diagnosis and treatment of HIV infection in children (diagnostic algorithm): • Questions of sensitivity and specificity of PCR tests are not specified in the CP • Issues of sensitivity and specificity of serological tests are specified in the order of the MHSD RK № 246.	**The 2016 WHO Guidelines, pages 28-41:** It is strongly recommended that HIV serological assays used for clinical diagnostic testing have a minimum sensitivity of 99% and specificity of 98% under quality-assured laboratory conditions (strong recommendation, moderate-quality evidence). **WHO, 2018, p . 40-41:** The indeterminate range suggested is currently estimated to be approximately equivalent to a cycle threshold of 33 on the Roche COBAS® Ampliprep/COBAS® TaqMan® HIV-1 Qualitative Test v2.0 assay.
Testing in special groups (adolescents, pregnant women, couples, and partners).	Order of the Minister of Health and Social Development of the Republic of Kazakhstan, dated June 23, 2015, No. 508 "On Approval of rules for mandatory confidential medical examination of people for HIV infection according to clinical and epidemiological indications," Section 2, "Procedure for conducting mandatory confidential medical examination of people for HIV infection according to clinical and epidemiological indications..." Page 8, CP "HIV infection in adults": • Immunochromatographic (enzyme-linked immunosorbent) analysis for HIV (ICA/ELISA) in pregnant women: upon registration, within 28-30 weeks (double examination)... • HIV testing of sexual partners of pregnant women while applying... • Rapid testing for HIV, followed by ELISA of pregnant women...	**The 2016 WHO Guidelines, page 42:** "HIV testing services, with linkages to prevention, treatment, and care, should be offered for adolescents from key populations in all settings (strong recommendation, very low-quality evidence)..." **Page 43:** "PITC for women should be considered a routine component of the package of care in all antenatal, childbirth, postpartum and pediatric care settings..." "The partners and family members (including children) of all people enrolled in HIV care and treatment should be offered HIV testing..." **Page 44:** "The greater emphasis is needed on reaching men with both HIV testing services and linkages to care and treatment..." "HIV testing services should be routinely offered to all key populations in the community, in closed settings such as prisons and facility-based settings..."
Diagnostic algorithms.	**Pages 9-10, Clinical protocol for the diagnosis and treatment of HIV infection in children** (diagnostic algorithm for children under 18 months) The algorithm for diagnosing HIV in infants differs from the WHO recommendation by the following: lack of HIV testing within 0-2 days from the date of birth, retesting with a negative result of the first test within 6 months from the date of birth (WHO - 9 months), questions on clinical observation of the infant between the first and second HIV tests were not specified. Annex 1 and Annex 2 of the Order of the MoH of RK, No. 246 dated April 22, 2015 (last amendment by the order of the MoH of RK, dated May 04, 2019, No.ҚР DSM-62): diagnostic algorithm in adults and children over 18 months. The algorithm for diagnosing HIV in infants differs from the 2016 WHO Guidelines by the use of IB to confirm the diagnosis and the use of rapid tests as a 0 test in an NGO setting.	**The 2016 WHO Guidelines, page 380,** Annex 8: A testing strategy for early infant diagnosis **The 2018 WHO Guidelines, pages 76-78 Annexes 4-5** **The 2016 WHO Guidelines, pages 378-379 Annexes 6-7:** A testing strategy for HIV diagnosis in high- and low-prevalence settings
Part 3. ARV drugs for HIV prevention		
Pre-exposure prophylaxis of HIV infection	Not specified in the regulatory documents of the Republic of Kazakhstan	**The 2016 WHO Guidelines, pages 52-61:** Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches (strong recommendation, high-quality evidence)... Recommended PrEP regimens: TDF, TDF + FTC

Algorithm and regimens of post-exposure prophylaxis for different population groups, including PMTCT.	**Page 8, the CP "HIV infection in adults":** RT for HIV, followed by ELISA for the injured person in an emergency.... **Pages 17-18,** the CP "HIV infection in adults": 8) In case of emergency (post-exposure prophylaxis) ... Preferred regimens: TDF + 3TC (or FTC) + LPV/r Alternative regimens: TDF + 3TC (or FTC) + RAL or DRV/r or EFV **Page 15, the CP "HIV Infection in adults":** Options to use ARV regimens for pregnant women who first sought help at the time of delivery. During child-birth: NVP 200 mg once and AZT 300 mg + 3TC 150 mg repeated every 12 hours, continuing after birth for 7 days. **Page 20, the CP "HIV infection in children":** · Preventive antiretroviral treatment is indicated for all children born to HIV-infected women from the first 6 hours and no later than 72 hours; · Recommended regimen: AZT (2 times a day) + NVP (once a day) during the first six weeks of life (the dose should be calculated depending on age and body weight); · Newborn children for whom contact with HIV was first established during the postpartum period should continue prophylaxis for another 6 weeks (12 weeks in total); · Appointment of ART in an emergency is conducted by an infectious disease specialist at the Center for the Prevention and Control of AIDS, in emergency situations, antiretroviral drugs are taken for 28 days. Preferred ART regimens for children ≤10 years: AZT + 3TC + LPV/r. Alternative ART regimens: ABC + 3TC or TDF + 3TC (or FTC) + RAL or DRV or EFV or NVP. Preferred ART regimens for children over 10 years: TDF + 3TC (or FTC) + LPV/r. Alternative ART regimens: TDF + 3TC (or FTC) + RAL or DRV/r or EFV.	**The 2016 WHO Guidelines, pages 61-63:** HIV PEP should be offered and initiated as early as possible in all individuals with an exposure that has the potential for HIV transmission, preferably within 72 hours. For individuals who may not be able to access services within this time, providers should consider the range of essential interventions and referrals that should be offered to clients presenting after 72 hours... Post-exposure prophylaxis ARV regimens for adults and adolescents: TDF + FTC + LPV/r or ATV/r for children ≤10 years: AZT + 3TC (or ABC + 3TC) + LPV/r PMTCT **The 2016 WHO Guidelines, page 120:** "Infants born to mothers with HIV who are at high risk of acquiring HIV should receive dual prophylaxis with AZT (twice daily) and NVP (once daily) for the first 6 weeks of life, whether they are breastfed or formula-fed (strong recommendation, moderate-quality evidence). Breastfed infants who are at high risk of acquiring HIV, and including those first identified as exposed to HIV during the postpartum period, should continue infant prophylaxis for an additional 6 weeks (total of 12 weeks of infant prophylaxis) using either AZT (twice daily) and NVP (once daily) or NVP alone (conditional recommendation, low-quality evidence). Infants of mothers who are receiving ART and are breastfeeding should receive 6 weeks of infant prophylaxis with daily NVP. If infants are receiving replacement feeding, they should be given 4–6 weeks of infant prophylaxis with daily NVP (or twice-daily AZT) (strong recommendation, moderate-quality evidence for breastfeeding infants; strong recommendation, low-quality evidence for infants receiving only replacement feeding)". **The 2018 WHO Guidelines, page 37 :** The preferred regimen is TDF + 3TC (or FTC) + DTG. Alternative drugs: ATV/r, DRV/r, LPV/r, and RAL. Children: Preferred regimen is AZT + 3TC + DTG. Alternative drugs: ABC + 3TC or TDF + 3TC (or FTC) + ATV/r, DRV/r, LPV/r and RAL.
Part 4. Antiretroviral therapy regimens		
When ART should be started, including recommendations for specific groups of patients (for whom urgent indication is recommended).	**Page 13, CP "HIV infection in adults":** ART should be initiated for patients with HIV infection, regardless of the clinical stage of the disease, with any number of CD4 cells, including all HIV-infected pregnant women. As a matter of priority, ART is given to all patients at stages 3-4 of HIV infection or patients with a CD4 cell count ≤ 350 cells/mm3. **Pages 12-13, CP "HIV infection in children":** ART should be initiated for all children with HIV, regardless of the clinical stage of the disease according to the WHO classification and with any number of CD4 cells. ART should be initiated first in all children <2 years or children <5 years with clinical stages 3-4 of HIV infection according to the WHO classification, or with a CD4 cell count of ≤750 cells/mm^3, or a percentage of CD4 cells <25%, and also for children 5 years and older with a clinical stage of HIV infection of 3-4 according to the WHO classification or a CD4 count ≤350 cells/mm^3.	**The 2016 WHO Guidelines, page 74:** "ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count (strong recommendation, moderate-quality evidence). As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤350 cells/mm3 (strong recommendation, moderate-quality evidence)..."

Choosing first-line drugs, including: • Preferences for fixed-dose combination (FDCs) drugs. • Refusal to use stavudine. • Use of DTG and EFV400 following the updated recommendations (2018, 2019). • Recommendations for use of dolutegravir in women of childbearing age and pregnant women.	**Page 13, CP "HIV infection in adults":** Preference is given to fixed-dose combined drugs with a single daily dose. First-line ART regimens **(CP, page 14):** Preferred 2 NRTI + 1 NNRTI regimen: 3TC (or FTC) + TDF + EFV Alternative regimen: 3TC + AZT + EFV, 3TC + AZT + NVP, 3TC (or FTC) + TDF + DTG, 3TC (or FTC) + TDF + NVP, 3TC (or FTC) + TDF + EFV400. Special circumstances: 3TC (or FTC) + ABC (or TDF) + DTG, LPV/r, DRV/r, DRV/s, RPV, ATV/r. DTG regimens are not included in the national CP for use in pregnant women. There is no recommendation for the use of stavudine.	**The 2016 WHO Guidelines, pages 98, 105:** "Fixed-dose combinations and once-daily regimens are preferred for antiretroviral therapy (strong recommendation, moderate-quality evidence) TDF + 3TC (or FTC) + EFV as a fixed-dose combination is recommended as the preferred option to initiate ART (strong recommendation, moderate-quality evidence). Alternative options: AZT + 3TC + EFV, AZT + 3TC + NVP, TDF + 3TC (or FTC) + NVP, TDF + 3TC (or FTC) + DTG or TDF + 3TC (or FTC) + EFV 400 mg/day. Special circumstances: regimens containing ABC and boosted PI. In all countries, d4T should be discontinued in first-line regimens due to its well-known metabolic toxicity (strong recommendation, moderate-quality evidence). Page 3 Update of recommendations on first- and second-line antiretroviral regimens. 2019 (WHO/CDS/HIV/19.15): Dolutegravir (DTG) in combination with a nucleoside reverse-transcriptase inhibitor (NRTI) backbone is recommended as the preferred first-line regimen for people living with HIV initiating ART. Efavirenz at a low dose (EFV 400 mg) in combination with an NRTI backbone is recommended as the alternative first-line regimen for adults and adolescents living with HIV initiating ARTc. Special circumstances: TDF + 3TC (or FTC) + EFV 600 mg, AZT + 3TC + EFV 600 mg, TDF + 3TC (or FTC) + PI/r, TDF + 3TC (or FTC) + RAL, TAF + 3TC (or FTC) + DTG, ABC + 3TC + DTG. **The 2019 WHO Guidelines, pages 6-8:** Provision of ART should follow a woman and human rights-centered approach. Women should be provided with information about the benefits and risks so that they can make an informed choice in favor of DTG or other ART.

First-line ART for special patient populations	**Page 13, CP "HIV infection in adults":** Special circumstances: 3TC (or FTC) + ABC (or TDF) + DTG, LPV/r, DRV/r, DRV/c, RPV, ATV/r **Pages 15-17, CP "HIV infection in adults":** • Pregnant women: TDF + 3TC (or FTC) + EFV. • Patients with an initial low (≤ 50 cells/mm3) CD4 + lymphocyte count: DTG or DRV/r or LPV/r in combination with ABC or TDF + 3TC or FTC. • Patients with cognitive abnormality: DTG or LPV/r or DRV/r in combination with AZT / 3TC. • Patients with chronic kidney disease: ABC or 3TC + EFV or NVP. • Patients with HIV co-infection and chronic hepatitis B, B + D are recommended: EFV or RPV in combination with TDF + 3TC or TDF/FTC; DTG boosted RTV PI (DRV/r or LPV/r) in combination with TDF + 3TC or TDF/FTC. • HIV infection and CHC: EFV, RPV or DTG in combination with ABC or TDF + 3TC or TDF/FTC; DTG or PI/b (LPV/r or DRV/r) in combination with ABC or TDF + 3TC or TDF/FTC. • Patients receiving TB drugs: 3TC or FTC and TDF in combination with EFV or DTG 50 mg 2 times a day. • Patients receiving methadone: if used together with NNRTIs or PIs, methadone concentration in plasma decreases: NVP or EFV - 50%, ETV - <10%, LPV/r - 50%, DRV/r - 15-25%	**The 2016 WHO Guidelines, page 98:** Special Circumstances: Regimens containing ABC and boosted PIs. **The 2019 WHO Guidelines, page 3 :** Special circumstances: TDF + 3TC (or FTC) + EFV 600 mg, AZT + 3TC + EFV 600 mg, TDF + 3TC (or FTC) + PI/r, TDF + 3TC (or FTC) + RAL, TAF + 3TC (or FTC) + DTG, ABC + 3TC + DTG.
Recommendations for breastfeeding of babies	**Page 20, CP "HIV infection in children":** A child born to an HIV-infected mother is not given its mother's breast and is switched from birth to formula feeding...	**The 2016 WHO Guidelines, page 125:** "National or subnational health authorities should decide whether health services will principally counsel and support mothers known to be HIV infected to either breastfeed and receive ARVs interventions or avoid all breastfeeding..."
Monitoring before and after starting ART	**Page 24, CP "HIV infection in adults":** • Viral load is determined before starting ART. In the future, VL should be measured for the first time no later than 3 months, then once every 6 months, when an undetectable VL level is reached. • The number of CD4 lymphocytes should be measured after 3 months, then every 6 months, if necessary, more often during the 1-st year of ART, then at least once a year (unless treatment is ineffective); • Laboratory tests must be conducted at least once every 6 months; • Testing for HLA-B*5701 allele before prescribing ART regimens containing ABC. • If the decrease in VL is absent a 6 months after the start of treatment by 1 log10 or a sequential twofold increase in VL after initial suppression, it is necessary to take a genotypic test to determine HIV resistance to antiretroviral drugs.	**The 2016 WHO Guidelines, pages 128-129 :** "Follow-up before ART: • CD4 cell count (every 6–12 months in circumstances where ART initiation is delayed) Receiving ART: • HIV viral load (at 6 months and 12 months after initiating ART and every 12 months thereafter). • CD4 cell count every 6 months until patients are stable on ART. Suspected treatment failure • Serum creatinine and eGFR for TDF. • Pregnancy test, especially for women of childbearing age not receiving family planning and on treatment with DTG or low-dose EFV

Recommendations for switching to second-line ART regimens, including special patient groups, and a preferred alternative regimen.	**Pages 18-19, CP "HIV infection in adults":** Treatment failure is defined as a consistently detectable viral load of more than 1000 copies/ml based on two consecutive measurements taken 2-4 weeks apart, but no earlier than six months after starting ARV use. Second-line ART regimens: Preferred regimens: AZT + 3TC + ATV/r, TDF + 3TC (or FTC) + LPV/r. Alternative regimens: AZT + 3TC + DRV/r, TDF + 3TC (or FTC) + DRV/r, ABC + 3TC (or FTC) + EFV or NVP ABC + 3TC (or FTC) + LPV/r or DRV/r, AZT (or ABC, or TDF) + 3TC (or FTC) DTG or RAL, AZT (or ABC, or TDF) + 3TC (or FTC) + LPV/r + RAL, TDF + 3TC (or FTC) + ETV. Specific patient groups are not specified.	**The 2016 WHO Guidelines, page 151:** "Second-line ART in adults should consist of two nucleoside reverse-transcriptase inhibitors (NRTIs) plus a ritonavir-boosted protease inhibitor (PI). The following sequence of second-line NRTI options is recommended: After failure on a TDF + 3TC (or FTC)-based first-line regimen, use AZT + 3TC as the NRTI backbone in second-line regimens. After failure on an AZT or d4T + 3TC-based first-line regimen, use TDF + 3TC (or FTC) as the NRTI backbone in second-line regimens. The use of NRTI backbones as a fixed-dose combination is recommended as the preferred approach (strong recommendation, moderate-quality evidence). Heat-stable fixed-dose combinations of ATV/r and LPV/r are the preferred boosted PI options for second-line ART (strong recommendation, moderate-quality evidence)." **The 2019 WHO Guidelines, page 11 :** Ineffective first-line regimens: TDF + 3TC (or FTC) + DTG, TDF + 3TC (or FTC) + EFV (or NVP), AZT + 3TC + EFV (or NVP). Switch to: AZT + 3TC + ATV/r (or LPV/r), AZT + 3TC + DTG, TDF + 3TC (or FTC) + DTG. Alternative second-line regimens: AZT + 3TC + DRV/r, AZT + 3TC + ATV/r (or LPV/r or DRV/r), TDF + 3TC (or FTC) + ATV/r (or LPV/r or DRV/r).
Recommendations for the third-line ARV drugs	**Page 19, CP "HIV infection in adults":** Third-line ART regimens: DRV/r + DTG (or RAL) ± 1-2 NRTI, DRV/r + 2NRTI ± NNRTI. Optimization of the regimen using the genotypic profile.	**The 2016 WHO Guidelines, page 159:** "National programs should develop policies for third-line ART (conditional recommendation, low-quality evidence). Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as INSTIs and second-generation NNRTIs and PIs (conditional recommendation, low-quality evidence). **Page 161:** DRV/r + DTG (or RAL) ± 1-2 NRTI, DRV/r + 2NRTI ± NNRTI. Optimization of the regimen using the genotypic profile "
Barriers to accessing key drugs recommended by WHO, when they are available (e.g., no registration, no inclusion in the list of vital and essential medicines or procurement lists, high price, etc.)	DTG is registered in the Republic of Kazakhstan, included in all regulations governing drug provision for patients within the guaranteed volume of free health care. The high price of the drug is a barrier. The cost of 1 tablet is 1604.67 tenge (4.2 USD), the cost of a package is 127 USD, the annual course is 1526 USD. According to the order of the Minister of Health of RK, dated August 29, No. ҚР DSM-117 "On approval of the list of medicines, medical devices within the guaranteed volume of free health care and in the system of compulsory social health insurance purchased from a Single distributor for 2020."	N/A

Part 5. Prevention and treatment of concomitant infections and diseases

Recommendations for the prevention and treatment of co-infections, primarily (but not limited to):

- HIV/HCV
- HIV/HBV
- HIV TB

ARV regimens for the treatment of co-infections are specified in the section "First-line ART for special groups of patients"

Page 25, CP "HIV infection in adults":

- Prophylaxis of TMP/SMX is prescribed for everyone with an advanced stage of HIV infection (stage 3-4 or with a CD4 level of ≤200 cells/mm3) for the prevention of Pneumocystis pneumonia and toxoplasmosis, all patients with active TB, regardless of their CD4 cell count...
- Tuberculosis (if active tuberculosis is excluded in the patient) - once prophylactic treatment with isoniazid (5 mg/kg) but not more than 0.3 g per day + pyridoxine at a dose of 25 mg/day for at least 6 months...
- Infection caused by MAC - in case of CD4 <50 cells/mm3 - azithromycin (1200 mg once a week).

The 2016 WHO Guidelines, page 93: "TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment (strong recommendation, high-quality evidence)."

The 2016 WHO Guidelines, page 119:

Summary of recommended ART regimens for children who needed treatment ...

The 2016 WHO Guidelines, page 147:

The most important interactions of ARVs with TB drugs, with drugs for the HCV treatment.

The 2016 WHO Guidelines, page 151:

"Second-line ART for HIV + TB, HIV + HBV"

The 2016 WHO Guidelines, page 192:

"Co-trimoxazole (CTX) prophylaxis is recommended for adults (including pregnant women) with severe or advanced HIV clinical disease (WHO stage 3 or 4) and/or with a CD4 count ≤350 cells/mm3 (strong recommendation, moderate-quality evidence).

In settings where malaria and/or severe bacterial infections (SBIs) are highly prevalent, co-trimoxazole prophylaxis should be initiated regardless of CD4 cell count or WHO stage..."

The 2016 WHO Guidelines, page 201:

"Adults and adolescents living with HIV should be screened with a clinical algorithm; those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT (strong recommendation, moderate-quality evidence). Adults and adolescents living with HIV who have an unknown or positive tuberculin skin test (TST) status and are unlikely to have active TB should receive at least six months of IPT as part of a comprehensive package of HIV care. IPT should be given to such individuals regardless of the degree of immunosuppression, and also to those on ART, those who have previously been treated for TB and pregnant women (strong recommendation, high-quality evidence)..."

The 2016 WHO Guidelines, page 205:

"The routine use of antifungal primary prophylaxis for cryptococcal disease in HIV-infected adults, adolescents, and children with a CD4 count less than 100 cells/mm3 and who are CrAg negative or where CrAg status is unknown is not recommended prior to ART initiation unless a prolonged delay in ART initiation is likely (strong recommendation, high-quality evidence)..."

The 2016 WHO Guidelines, page 208:

Management tactics for patients with hepatitis B and C.

The 2016 WHO Guidelines, page 210:

Management of patients with malaria.

The 2016 WHO Guidelines, page 212:

Management of patients with STIs and cervical cancer.

Prevention and treatment of relevant non-communicable diseases: • Cardiovascular diseases • Depression • Diseases of the central nervous system • Kidney diseases • Substance use	**Page 30 KP "HIV infection in adults":** Diagnosis of cognitive (neurocognitive) disorders: It is advisable to assess cognitive disorders (cognitive functions) in all HIV-infected patients without confounding factors (severe psychiatric diseases, abuse of psychoactive substances, including alcohol, current opportunistic infections of the central nervous system, other neurological diseases) within 6 months since the diagnosis was made.	**The 2016 WHO Guidelines, pages 215-225:** "Assessment and management of non-communicable diseases."
Part 6. Health service provision		
The provision of health services, including but not limited to: • Recommendations for the decentralization of services. • Recommendations for redistribution and delegation of services. • Recommendations for integration of services.	Not specified in the national CP.	**The 2016 WHO Guidelines, page 238:** This chapter provides guidance in three service delivery areas: • Differentiated care • Recommendations to strengthen the continuum of treatment and care. • Considerations for continuity and high quality of service delivery

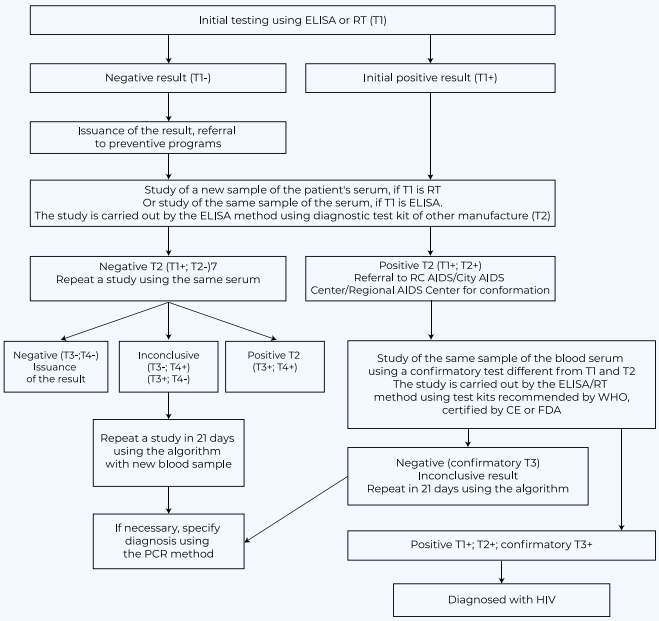
Kyrgyzstan

Part 1. Basic information	
Name of the current version of the document and the link to it.	Clinical protocols on HIV infection for outpatient and inpatient healthcare levels Other HIV protocols
Year of the current version.	2017
The normative document number and its status (order, resolution, if applicable).	Order of the MoH of KR, No. 903, dated October 10, 2017
Legal status of recommendations: mandatory or advisory (What additional documents govern the need for recommendations).	Protocol status is mandatory. Order of the MoH of KR, No 490, dated September 4, 2006: the establishment of a sustainable system for the development, implementation, and monitoring of Clinical guidelines/Clinical protocols and further promotion of EBM principles in practical health care, education, and science. This document is currently being revised.
Frequency of the document revision (Is it defined? What documents regulate this?).	Revision of Clinical Protocols is carried out as fundamentally new data become available.
Level of evidence (description of the applicable system).	Evidence level is according to GRADE and strength of recommendation.
Members of the editorial board (Are representatives of NGOs/ patient organizations included?).	The team for the development of current protocols included scientific and medical professionals, pharmacology and diagnostics specialists, healthcare administrators, and representatives of non-governmental organizations.
List and a brief description of documents that additionally regulate the use of ARVs in the country, including the following documents, but not limited to: · Laws governing the nature of supplying the ARVs (free of charge/paid, by prepaid medical care plan or at the expense of a special national program, etc.); · Lists of vital and essential medicines; · Lists of medicines to be procured at the expense of different budgets; · Treatment standards, etc.	Access to HIV treatment is regulated by separate legislative acts (Law on HIV/AIDS, dated August 13, 2005, No. 149 (as amended by the Laws of KR, dated June 13, 2011, No. 44, April 29, 2016 No. 52, May 4, 2017, No. 74), the Government Program to Overcome HIV infection in the Kyrgyz Republic for 2017-2021, dated December 30, 2017, No.852, National Healthcare Reform Program in the Kyrgyz Republic "Den Sooluk" for 2012-2018).

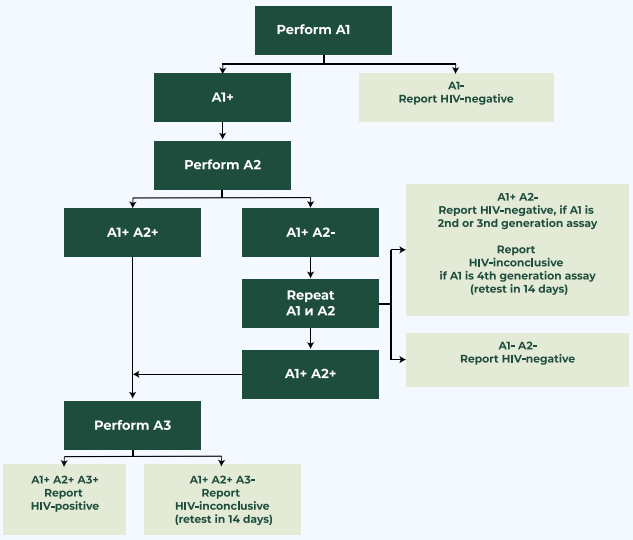
Page and quote from national protocols	Comment	Link to relevant WHO recommendation, page, document, quote
Part 2. Diagnostic recommendations		
Page 19 "If the result is positive, appoint repeated counseling"	Additionally in the Instruction "Laboratory diagnostics of HIV infection in the Kyrgyz Republic", approved by order of the MoH of KR, No. 303, dated April 28, 2018, p. 3.3. "Retesting to verify the diagnosis of HIV infection before starting ART" brought in line.	**The 2016 WHO Guidelines, page 19:** "National programs should retest all people newly and previously diagnosed with HIV before they enroll in care and initiate ART."
Page 15 . The national policy and practice on HTC in HIV infection, in accordance with national legislation in KR, provides access to testing services and the confidentiality of their results. HTC is of great importance in terms of primary and secondary prevention of HIV infection, it is an important component of work on treatment, care, and support of PLHIV.	This section is in full compliance with the WHO recommendations.	**The 2016 WHO Guidelines, page 18:** HIV testing is the gateway to HIV prevention, treatment, care, and other support services. HIV testing services (HTS) refer to the full range of services that should be provided with HIV testing, including counseling (pre-test information and post-test counseling); linkage to appropriate HIV prevention, treatment and care, and other clinical services; and coordination with laboratory services to support quality assurance (QA) and the delivery of accurate results.

Page 22. Application of rapid tests to expand access to HTC services. The implementation of rapid HIV tests that are highly sensitive and specific and do not require sophisticated laboratory equipment is an important achievement in public health. Currently, such tests are becoming more and more widely used, including NGOs.	Additionally in the Instruction "Laboratory diagnostics of HIV infection in the Kyrgyz Republic", approved by order of the MoH of KR, No. 303, dated April 28, 2018. 3.1. Testing for HIV infection using rapid tests. Rapid tests in the Kyrgyz Republic are used in healthcare and non-healthcare (SMC, TB, NGO, SSEP, SEP, anonymous offices, trust rooms, etc.) facilities when citizens apply for an HIV test. RT shall be conducted only by specialists who have undergone special training and received an appropriate certificate. - brought in line.	**Page 25.** Lay providers who are trained and supervised can independently conduct safe and effective HIV testing using rapid diagnostic tests (RDTs) (strong recommendation, moderate-quality evidence).
Page 19. To expand access to HTC services, it is necessary to introduce health care provider-initiated testing and counseling (PITC) for patients with suspected HIV infection and those whose professional activities require a mandatory medical examination for HIV.	It is in full compliance with WHO recommendations.	**Page 26.** Facility-based HIV testing services – often referred to as provider-initiated testing and counseling (PITC) – are those that are routinely offered in a health facility or by private medical practitioners. They may be offered in a range of clinical settings, depending on the type of epidemic, the population served, and the capacity of the facility.
Page 286. Diagnosis of HIV infection in an infant is conducted by PCR for HIV DNA within 48 hours after birth. A positive PCR result is the basis for a preliminary diagnosis of HIV infection and an indication of the need to initiate ART. Regardless of the outcome, the second test should be repeated at 4-6 weeks of age.	It is in full compliance with WHO recommendations.	**Page 29.** In infants and children undergoing virological testing, the following assays (and respective specimen types) are strongly recommended for use: HIV DNA on whole blood specimen or DBS. "...It is strongly recommended that all HIV-exposed infants have HIV virological testing at 4–6 weeks of age or the earliest opportunity thereafter (strong recommendation, high-quality evidence). In infants with an initial positive virological test result, it is strongly recommended that ART be started without delay and, at the same time, a second specimen be collected to confirm the initial positive virological test result. Do not delay ART. Immediate initiation of ART saves lives and should not be delayed while waiting for the results of the confirmatory test (strong recommendation, high-quality evidence).
Page 16. During the counseling session, it is necessary to discuss important issues related to the specifics of the high-risk group for HIV infection, to which the person receiving the test belongs (PWID, CSW, MSM, persons in PDL, etc.). During the counseling, couples and partners are encouraged to offer voluntary group, individual or couple counseling, HIV testing, and support while discovering HIV status. **Page 21.** Medical examination of children and adolescents and persons recognized as legally incapacitated must be conducted in the presence of the written consent of their legal representatives, who have the right to be present during the medical examination for HIV. **Page 280.** HIV counseling and testing for the pregnant woman and her sexual partner is vital to prevent vertical transmission of HIV. **Page 279**. ART should be initiated by all HIV-positive pregnant and breastfeeding women, regardless of the clinical stage of the disease, gestational age, and any CD4 cell count.	There are no separate recommendations for adolescents. Recommendations for pregnant women and partners comply.	**Page 42:** "HIV testing services, with linkages to prevention, treatment, and care, should be offered for adolescents from key populations in all settings (strong recommendation, very low-quality evidence). Adolescents with HIV should be counseled about the potential benefits and risks of disclosure of their HIV status, and empowered and supported to determine if, when, how and to whom to disclose (conditional recommendation, very low-quality evidence). **Page 43.** The routine offer of HIV testing at the first ANC visit has been critical to the roll-out of universal ART for all pregnant women living with HIV. **Page 44.** Couples and partners should be offered voluntary HIV testing services with support for mutual disclosure. This applies also to couples and partners from key populations (strong recommendation, low-quality evidence).

Chart 2. HIV testing algorithm



The HIV testing algorithm fully complies with the WHO recommendations:



7 Linear scheme of permutation of repeated results:

T1(+); T2(-); T3(-); T4(-) – Negative

T1(+); T2(-); T3(-); T4(+) – Inconclusive (Repeat in 21 days)

T1(+); T2(-); T3(+); T4(-) – Inconclusive (Repeat in 21 days)

T1(+); T2(-); T3(+); T4(+) – Positive (Repeat for confirmation using T2- positive algorithm)

Part 3. ARV drugs for HIV prevention

Page 66. As part of comprehensive HIV prevention, people at increased risk of HIV infection are encouraged to use oral TDF-containing ARVs for pre-exposure prophylaxis to provide additional protection against HIV infection (Strong recommendation, high-quality evidence).	Recommendations on TDF-based PrEP comply with the WHO guidelines	**Page 52.** Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches (strong recommendation, high-quality evidence).
Page 56. Contacts for which HIV PEP is justified: body fluids - blood, blood-stained saliva, breast milk, genital secretions, cerebrospinal, amniotic, peritoneal, synovial, pericardial, or pleural secretions. **Page 59.** PEP should be started within the first 2 hours and no later than 72 hours after probable exposure to HIV, a duration of 28 days. · TDF + 3TC (or FTC) is recommended as the preferred backbone regimen for HIV PEP for adults and adolescents (Strong recommendation, low-quality evidence). · LPV/r or ATV/r is recommended as the preferred third drug (Conditional recommendation, very low-quality evidence).	PEP following the WHO Guidelines specify indications, timing, and regimens of ART with recommendations: NVP should not be used for PEP in adults, adolescents, and older children due to the risk of life-threatening serious adverse events associated with the use of this drug in HIV negative adults.	**Pages 61, 62.** HIV PEP should be offered and initiated as early as possible in all individuals with an exposure that has the potential for HIV transmission, preferably within 72 hours. For individuals who may not be able to access services within this time, providers should consider the range of essential interventions and referrals that should be offered to clients presenting after 72 hours. Post-exposure prophylaxis ARV regimens for adults and adolescents: · TDF + 3TC (or FTC) is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis for adults and adolescents (strong recommendation, low-quality evidence). · LPV/r or ATV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for adults and adolescents (conditional recommendation, very low-quality evidence). Where available, RAL, DRV/r, or EFV can be considered as alternative options.

Alternative PEP regimens: • TDF/FTC/EFV; AZT + 3TC + LPV/r • If possible, RAL, DRV/r may be considered as alternatives. • EFV is widely used as a third drug. • AZT + 3TC is recommended as the preferred backbone regimen for HIV PEP for children 10 years of age and younger. • LPV/r is recommended as the preferred third drug (Conditional recommendation, very low-quality evidence) • ABC + 3TC or TDF + 3TC (or FTC) + LPV/r can be considered as alternative regimen. • An age-appropriate alternative regimen can be identified among ATV/r, RAL, DRV, EFV, and NVP. • NVP should be used in premature infants and infants up to 2 weeks of age when oral prophylaxis with liquid LPV/r cannot be used.		Post-exposure prophylaxis ARV regimens for children ≤10 years: AZT + 3TC is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis for children aged 10 years and younger. ABC + 3TC or TDF + 3TC (or FTC) can be considered as alternative regimens (strong recommendation, low-quality evidence). LPV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for children younger than 10 years (conditional recommendation, very low-quality evidence). An age-appropriate alternative regimen can be identified among ATV/r, RAL, DRV, EFV, and NVP.
Part 4. Antiretroviral therapy regimens		
Page 76. ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count. **In priority order:** ART should be initiated in all patients with advanced clinical stage of HIV infection (clinical stage 3-4 according to the WHO classification) or patients with CD4 cell count ≤350 cells/mm3. **Page 267.** ART should be initiated in all HIV-positive pregnant and breastfeeding women regardless of the clinical stage of the disease, gestational age and with any CD4 cell count, and continue lifelong. **Page 284.** ART should be initiated in all infants and children under 15 years of age living with HIV regardless of the clinical stage of the disease according to the WHO classification and for any CD4 cell count. **Page 124.** ART should be prescribed for all PLHIV with active TB regardless of CD4 cell count TB treatment is started first, and then ART is prescribed as soon as possible (in the first 2-8 weeks of treatment). HIV-positive patients with profound immunosuppression (CD4 cell count less than 50 cells/mm3) should receive ART within the first two weeks of initiating TB treatment. If TB meningitis is present, the initiation of ART should be postponed until the end of the intensive TB care phase. In patients on TB treatment, EFV is the preferred NNRTI in ART with two NRTIs (grade A, strong recommendation).	Indications for initiating ART and first-, second- and third-line regimens for adults, adolescents, and children are fully in line with the WHO Guidelines, including special cases.	**The 2016 WHO Guidelines, page 74.** ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count (strong recommendation, moderate-quality evidence). As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤350 cells/mm3 (strong recommendation, moderate-quality evidence). **Page 81.** ART should be initiated in all pregnant and breastfeeding women living with HIV regardless of WHO clinical stage and at any CD4 cell count and continued lifelong (strong recommendation, moderate-quality evidence). **Page 89.** ART should be initiated in all children living with HIV, regardless of WHO clinical stage or at any CD4 cell count: Infants diagnosed in the first year of life (strong recommendation, moderate-quality evidence); Children living with HIV 1year to younger than 10 years (conditional recommendation, low-quality evidence). **Page 93.** ART should be started in all TB patients living with HIV, regardless of CD4 cell count (strong recommendation, high-quality evidence). TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment (strong recommendation, high-quality evidence) HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm3) should receive ART within the first two weeks of initiating TB treatment. ART should be started in any child with active TB disease as soon as possible and within 8 weeks following the initiation of antituberculosis treatment, regardless of the CD4 cell count and clinical stage (strong recommendation, low-quality evidence).

Page 77. Separate groups of patients. Adolescents and adult patients: TDF + 3TC (or FTC) + EFV. Pregnant and breastfeeding women: TDF + 3TC (or FTC) + EFV. HIV/TB patients: TDF + 3TC (or FTC) + EFV. HIV/HBV patients: TDF + 3TC (or FTC) + EFV. HIV/HCV patients: TDF + 3TC (or FTC) + EFV. PLHIV PWID: TDF + 3TC (or FTC) + EFV. Children under 3 rears: ABC (or AZT) + 3TC + LPV/r. Children from 3 years to less than 10 years: ABC + 3TC + EFV. Stavudine is not included in ART regimens. DTG: data on safety and efficacy in pregnant women and adolescents under 12 years are not yet available.	The section on ART in special cases contains regimens that comply with the WHO Guidelines.	**Page 97.** Adult patients: TDF + 3TC (or FTC) + EFV as a fixed-dose combination is recommended as the preferred option to initiate ART (strong recommendation, moderate-quality evidence). Pregnant or breastfeeding women: TDF + 3TC (or FTC) + EFV. Adolescents: TDF + 3TC (or FTC) + EFV. Children 3 years to less than 10 years: ABC + 3TC + EFV. Children less than 3 years: ABC (or AZT) + 3TC + LPV/r. In all countries, d4T should be discontinued in first-line regimens due to its well-known metabolic toxicity (strong recommendation, moderate quality of evidence). Data on the safety and efficacy of DTG and EFV at a low dose of 400 mg per day in pregnant and breastfeeding women and in TB co-infection are not yet available.
Page 269. Exclusive breastfeeding with the mother on ART is recommended. HIV-positive mothers must exclusively breastfeed their babies for 6 months of life, after which appropriate complementary foods are introduced and breastfeeding continues for the first 12 months of life. Exclusive breastfeeding means the use of exclusively breast milk without water, milk formulas. When detecting HIV infection in a child by early infant diagnosis (EID), breastfeeding is recommended as long as possible and acceptable.	The CP includes the WHO recommendations on exclusive breastfeeding.	**Page 125.** National or subnational health authorities should decide whether health services will principally counsel and support mothers known to be HIV infected to either breastfeed and receive ARVs interventions or avoid all breastfeeding. In settings where national authorities have decided that maternal and child health services will principally promote and support breastfeeding and antiretroviral interventions as the strategy that will most likely give infants born to mothers known to be HIV infected the greatest chance of HIV-free survival, mothers known to be infected with HIV should exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life. Breastfeeding should then stop only once a nutritionally adequate and safe diet without breast milk can be provided (strong recommendation, high-quality evidence for the first 6 months; low-quality evidence for the recommendation of 12 months).
Page 78. VL can be conducted before initiating ART, in 6 and 12 months after starting ART, then every 12 months if the condition is stable. In case of an unstable condition, the frequency of monitoring for VL is 1 time in 3 months. When routine VL monitoring with stable ART, CD4 count monitoring can be discontinued. If routine VL testing is not possible, CD4 counts and clinical monitoring are used to diagnose ART failure.	For monitoring the effectiveness of ART, the CP determines viral load by the main indicator and the timing of determination is in accordance with the WHO Guidelines.	**Page 129.** Routine viral load monitoring can be carried out at 6 months, at 12 months, and then every 12 months thereafter if the patient is stable on ART to synchronize with routine monitoring and evaluation reporting (conditional recommendation, very low-quality evidence). In settings where routine viral load monitoring is available, CD4 cell count monitoring can be stopped in individuals who are stable on ART and virally suppressed (conditional recommendation, low-quality evidence).

Page 81. The strategy of switching to the second-line regimen. Viral load monitoring is conducted to assess regularly the effectiveness of ART and if clinical and immunological failure is suspected. If the viral load is above 1000 copies/mL, adherence assessment and viral load retest are conducted after 3 months. With a decrease in VL less than 1000 copies/mL, it is recommended to continue the first-line regimen. If the VL is still over 1000 copies/mL, it is recommended to switch to the second-line regimen.

Page 82. Second-line ART regimens:

Adults and adolescents, including pregnant or breastfeeding women: 2 NRTIs + ATV/r or LPV/r.

NRTI basics: TDF + 3TC (or FTC), ABC + 3TC, AZT + 3TC.

Alternative regimen: 2 NRTIs + DRV/r.

HIV/TB co-infection: 2NRTIs + LPV/r double dose (800/200 mg twice daily).

HIV HBV co-infection: AZT + TDF + 3TC (or FTC) + (ATV/r or LPV/r).

Page 290. Second-line ART regimens.

Children under 3 years:

- AZT (or ABC) + 3TC + RAL,
- AZT + 3TC + ATV/r or LPV/r.

Children over 3 years and under 10 years old:

- AZT (or ABC) + 3TC + EFV or RAL,
- ABC or TDF + 3TC + EFV or RAL,
- AZT (or ABC) + 3TC + ATV/r or LPV/r.

Children from 10 to 15 years old: 2 NRTIs + ATV/r or LPV/r.

The strategy of switching to second-line ART is presented in the form of a diagram describing the stages of examination and subsequent actions in accordance with the WHO Guidelines.

The CP does not specify that basic NRTI therapy in the form of a fixed-dose combination is preferable, although in practice fixed-dose combination ARVs are used and they are included in the EML: ABC/3TC, 3TC/ZDV, FTC/TDF, EFV/FTC/TDF.

Stavudine in the CP is not used in ART regimens.

Page 129. Viral load is recommended as the preferred monitoring approach to diagnose and confirm treatment failure (strong recommendation, low-quality evidence).

Viral failure is defined by a persistently detectable viral load exceeding 1000 copies/mL (that is, two consecutive viral load measurements within a 3-month interval with adherence support between measurements) after at least 6 months of starting a new ART regimen.

Page 152. Second-line ART in adults should consist of two nucleoside reverse-transcriptase inhibitors (NRTIs) plus a ritonavir-boosted protease inhibitor (PI). The following sequence of second-line NRTI options is recommended:

- After failure on a TDF + 3TC (or FTC)-based first-line regimen, use AZT + 3TC as the NRTI backbone in second-line regimens.
- After failure on an AZT or d4T + 3TC-based first-line regimen, use TDF + 3TC (or FTC) as the NRTI backbone in second-line regimens.

The use of NRTI backbones as a fixed-dose combination is recommended as the preferred approach (strong recommendation, moderate-quality evidence).

Heat-stable fixed-dose combinations of ATV/r and LPV/r are the preferred boosted PI options for second-line ART (strong recommendation, moderate-quality evidence).

Heat-stable fixed-dose combinations of DRV/r can be used as an alternative boosted PI option for second-line ART (conditional recommendation, low-quality evidence).

A combination of RAL plus LPV/r can be used as an alterna¬tive second-line ART regimen (conditional recommendation, low-quality evidence).

P. 156. Following the failure of first-line LPV / r-based therapy, children under 3 years of age should be switched to a second-line regimen based on RAL (conditional recommendation, very low quality of evidence).

After the failure of LPV / r-based first-line therapy, children over 3 years of age should be switched to a second-line regimen containing two NRTIs plus EFV or RAL (conditional recommendation, very low quality of evidence).

After the failure of first-line NNRTI-based therapy, children should be switched to a boosted PI regimen. LPV / r or ATV / r are preferred.

After the failure of first-line therapy that includes ABC or TDF + 3TC (or FTC), AZT + 3TC is the preferred baseline NRTI treatment option for the second line (strong recommendation, low-quality evidence)

After the failure of first-line therapy including AZT or d4T + 3TC (or FTC), ABC or TDF + 3TC (or FTC) is the preferred baseline NRTI treatment option for second-line ART (strong recommendation, low quality of evidence).

Page 83. Third-line ART regimens should include new drugs with minimal risk of cross-resistance to previously used drugs, such as second-generation NNRTIs and INSTI, and PIs (conditional recommendation, low-quality evidence). Patients on a failing second-line regimen with no new ARV drug options should continue with a tolerated regimen (conditional recommendation, very low-quality evidence). Third-line ART regimens for adults and adolescents, including pregnant and breastfeeding women: · DRV/r + DTG ± 1–2 NRTI, · DRV/r + 2 NRTI ± NNRTI. Optimization of the regimen using the genotypic profile.	Third-line ART regimens are in full accordance with the WHO Guidelines.	**Page 159**. Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as INSTIs and second-generation NNRTIs and PIs (conditional recommendation, low-quality evidence). Patients on a failing second-line regimen with no new ARV drug options should continue with a tolerated regimen (conditional recommendation, very low-quality evidence). **Page 161.** Third-line ART regimens for adults and adolescents, including pregnant and breastfeeding women: · DRV/r + DTG (or RAL) ± 1-2 NRTI, · DRV/r + 2NRTI ± NNRTI. · Optimization of the regimen using the genotypic profile Third-line ART regimens for children 0-10 years: · RAL (or DTG) + 2 NRTIs · DRV/r + 2 NRTI · DRV/r + RAL (or DTG) ± 1–2 NRTIs
Note: The drugs provided for in the CP 2017 were included in the EML. The full provision of ARV drugs using the GF grants was carried out until 2018; since 2018, the purchase of ARV drugs is carried out at the expense of the state budget and partially by the GF. List of ARV drugs included in the EML: · NRTI: ABC, 3TC, ZDV, TDF. · NNRTI: EFV, NVP. · IP: LPV r, RTV, ATV, DRV, SQV. · INSTI: DTG. Fixed-dose combinations: ABC/3TC, EFV/TDF/FTC, TDF/FTC, 3TC/NVP/d4T, 3TC/NVP/ZDV, ZDV/ 3TC.		
Part 5. Prevention and treatment of concomitant infections and diseases		
Recommendations for the prevention and treatment of co-infections, primarily (but not limited to): **HIV/hepatitis C virus (HCV).** **Page 136.** All persons with HIV/HCV co-infection should be considered candidates for HCV treatment. In HCV patients without hepatic fibrosis and HIV with severe immunosuppression (CD4 lymphocyte count below 200 cells/mm3), it is recommended to firstly initiate HIV treatment and achieve clinical stabilization of HIV infection with ART and then switch to HCV treatment. Hepatitis C in PLHIV should be treated with the same regimens, following the same rules as for patients with monoinfection of CHCV. Antiviral therapy regimens in the presence of compensated and decompensated liver cirrhosis as a result of CHCV in PLHIV.	**Annex 7. Page 135.** Management of patients with HIV and VH co-infection. The content of the CP complies with the WHO Guidelines. Detailed data on clinical and laboratory criteria of hepatitis C are presented, it is specified a table with antiviral therapy regimen for hepatitis C in PLHIV with direct-acting antiviral drugs (DAAs): DAC + SOF; DAC + SOF + RBV; LED + SOF; LED + SOF + RBV; SOF + RBV, and treatment monitoring. A table is provided to track the interaction between DAA and ART. The CP specifies the tactics of managing special cases: HIV/HCV/HBV; HIV/HCV/TB Direct-acting antiviral drugs are included in the EML.	Recommendations for the prevention and treatment of co-infections: **Page 209. HIV/HCV.** Clinical stabilization of HIV disease with ART is advisable prior to start treatment for HCV, especially in people with advanced immunosuppression (CD4 count below 200 cells/mm3). The newer, all-oral direct-acting antiviral HCV regimens (DAAs) produce similar rates of sustained virological response regardless of HIV status.
HIV/HBV. Page 142. All patients with HIV/HBV co-infection, including those with hepatic cirrhosis due to HBV, should start ART regardless of the clinical stage of HIV infection and for any CD4 cell count. All patients with HBV/HIV co-infection should be prescribed ART with dual activity against HIV and HBV, including: TDF 300 mg or TAF 25 mg + 3TC 150 mg or FTC 200 mg + EFV 600 mg.	The HIV/HBV section provides information on vaccination along with relevant WHO recommendations. Principles of HBV vaccination of PLHIV: Response to hepatitis B vaccination is less marked in PLHIV or with low CD4 cell count. In this connection, a regimen with four double doses (40 µg) of the vaccine is recommended: 0-1-6-12 months.	**Page 208. HIV/HBV** All people living with HIV - adults, adolescents, and children with chronic hepatitis B and clinical evidence of cirrhosis (or cirrhosis based on the non-invasive APRI test score >2 in adults) should be treated regardless of alanine aminotransferase (ALT) levels, hepatitis B e antigen (HBeAg) status or HBV DNA levels. The recommended NRTI drugs for ART – TDF with 3TC or FTC – are active against HBV. If ARV drugs need to be changed because of HIV drug resistance or toxicity, then TDF with 3TC or FTC should be continued together with the new ARV drugs.

HIV/TB. Page 112. As an initial diagnostic test in adults and children with suspected HIV-associated TB or MDR-TB, Xpert MTB/RIF should be used instead of standard microscopy, culture, and drug susceptibility testing (grade C, strong recommendation). Xpert MTB/RIF should be preferred over standard microscopy or culture as the initial diagnostic test for CSF specimens in patients with suspected TB meningitis (grade C, strong recommendation). Xpert MTB/RIF can be used in place of conventional methods (including standard microscopy, culture, or histological examination) for testing selected specimens (lymph nodes and other tissues) in patients with extrapulmonary TB (grade D, strong recommendation). LF-LAM should not be used to diagnose TB, unless it is in HIV-positive people with low CD4 counts or seriously ill patients (grade C, strong recommendation) / **Page 113.** The LF-LAM method can be used as an assisted method for the diagnosis of TB in hospitalized PLHIV with signs and symptoms of TB (pulmonary or extrapulmonary) with a CD4 lymphocyte count of fewer than 100 cells/mm3 or in seriously ill patients with a low or unknown cell number (level D, strong recommendation). The LF-LAM method should not be used as a screening test for active TB (grade C, strong recommendation).	All new WHO recommendations on HIV/TB diagnosis included in the CP **Pages 109-111.** A detailed description of TB diagnosis in PLHIV is presented: · medical examination · testing one sputum or other biological sample using Xpert MTB/RIF; if MTB/RIF for TB is positive, carry out the Hain Genotype MTBDRs/l assay; · taking 2 samples for sputum bacterioscopy; · other bacteriological tests (examination of sputum by inoculation for culture isolation) of two sputum samples taken even on the same day are carried out if it is not possible to use the Xpert MTB/RIF test system; · chest x-ray; · People with evidence of extrapulmonary TB should have microbiological examination (Xpert MTB/RIF or culture of the pathogen) of material obtained by aspiration or tissue biopsy. In patients with signs of disseminated infection or progressive immunodeficiency, blood culture for mycobacteria may be helpful, and if extrapulmonary TB is suspected, any additional testing, including computed tomography and other methods (if available), is recommended. TB treatment issues are included in Annex 5 on Antiretroviral Therapy.	**Page 197. HIV/TB.** Xpert MTB/RIF should be used rather than conventional microscopy, culture and drug susceptibility testing (DST) as the initial diagnostic test in adults and children suspected of having multidrug-resistant TB (MDR-TB) or HIV-associated TB (strong recommendation, adults: high-quality evidence; children: very low-quality evidence). Xpert MTB/RIF should be used in preference to conventional microscopy and culture as the initial diagnostic test for cerebrospinal fluid specimens from patients suspected of having TB meningitis (strong recommendation, very low-quality evidence). Xpert MTB/RIF may be used as a replacement test for usual practice (including conventional microscopy, culture or histopathology) for testing specific non-respiratory specimens (lymph nodes and other tissues) from patients suspected of having extrapulmonary TB (conditional recommendation, very low-quality evidence). Except as specifically described below for people with HIV infection with low CD4 counts or who are seriously ill, urine lateral flow (LF)-LAM should not be used for the diagnosis of TB (strong recommendation, low-quality evidence). LF-LAM may be used to assist in the diagnosis of active TB in adult inpatients living with HIV, with signs and symptoms of TB (pulmonary and/or extrapulmonary), who have a CD4 count less than or equal to 100 cells/mm3, or people living with HIV who are seriously ill, regardless of CD4 cell count or with unknown CD4 cell count (conditional recommendation, low-quality evidence). LF-LAM should not be used as a screening test for active TB (strong recommendation, low-quality evidence). **Page 93.** ART should be started in all TB patients living with HIV, regardless of CD4 cell count (strong recommendation, high-quality evidence). · TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment (strong recommendation, high-quality evidence). · HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm3) should receive ART within the first two weeks of initiating TB treatment. · ART should be started in any child with active TB disease as soon as possible and within 8 weeks following the initiation of antituberculosis treatment, regardless of the CD4 cell count and clinical stage (strong recommendation, low-quality evidence).
Prevention and treatment of relevant non-communicable diseases: · Cardiovascular disease · Depression · Diseases of the central nervous system · Kidney disease · Use of psychoactive substances	A separate addendum for the prevention and treatment of noncommunicable diseases has not been developed. Annex 5. “Antiretroviral Therapy in Adults and Adolescents” has a section on pages 71-73. “5. Assessment of comorbidities and conditions before initiating ART”, which contains criteria for the diagnosis and detection of diseases of the cardiovascular system and kidneys providing a risk assessment using online scales, as well as diseases of the lungs, liver, and bones. Screening questionnaires have been proposed to identify neurocognitive disorders and depression. Screening methods for cervical cancer in women over 40. Clinical screening for tuberculosis, STIs.	

Page 222. Annex 11. "Immunization of people living with HIV" contains: Rationale, basic principles of immunization and the table "Immunization of people living with HIV in the framework of the National preventive immunization calendar of the Kyrgyz Republic" with optimal timing: BCG, IPV (inactivated poliomyelitis vaccine), OPV (live), HBV (inactivated), DTaP (inactivated), ADS (inactivated), ADS-M (inactivated)		**Page 214. 5.2.7** Vaccines for people living with HIV In general, HIV-exposed infants, children, and adolescents with HIV should receive all vaccines under routine vaccination according to recommended national immunization schedules
Page 210. Appendix 10 "HIV in people who inject drugs: treatment and care" presents the following prevention, treatment and care measures for HIV-infected PWID: opioid substitution therapy; HIV counseling and testing (Annex 1); ART (Annex 5); prevention and treatment of sexually transmitted infections (Annex 12); condom support programs; prevention and treatment of viral hepatitis (Annex 7); prevention, diagnosis, and treatment of TB (Annex 6).	Harm reduction programs for PWID, in particular, NSP; targeted information and education activities to promote behavior change are not specified in the KP.	**Page 221**. It is recommended to use a comprehensive package of nine interventions for HIV prevention, treatment, and care for people who inject drugs; these are needle and syringe programs, OST, HIV testing and counseling, ART, preventing and treating STIs, condom programs, targeted behavior change communication, preventing and treating viral hepatitis and preventing, diagnosing and treating TB.
Part 6. Health service delivery		
The Government Program to Overcome HIV Infection in the Kyrgyz Republic for 2017-2021 includes strategies for decentralization, redistribution, delegation, and integration of services: "To achieve the goal and objectives set for the period until 2021, targeted actions will be taken in three strategic directions. This approach will ensure maximum effect at all levels of comprehensive health services delivery, coordinate the activities of the health sector with other government departments and services, with the non-governmental sector and communities of people affected by HIV, and increase the effectiveness of international technical and financial assistance."	The CP does not include the Recommendations on decentralization, redistribution, delegation, and integration of services.	

North Macedonia

In the Republic of North Macedonia there are no comprehensive national guidelines for the prevention and treatment of HIV infection. However, there is one official document at the national level that is meant to direct certain aspects in the medical treatment and the prevention of HIV. Some aspects of HIV care and treatment that the WHO Guidelines address are covered in other national or clinical-level protocols or guidelines. This analysis compares the WHO Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection from 2016 — and the updates of 2018 and 2019 — with all existing relevant recommendations in several different official documents that the consultants managed to identify.

The present analysis took into consideration the main documents existing in the Republic of North Macedonia that provide directions, guidelines or recommendations regarding the treatment and care of HIV infection, comparing them to WHO Guidelines from 2016 and the up-dates of 2018 and 2019. In addition, the consultants considered documents that additionally regulate the use and the supply of ARVs in the country, including in particular the Law on Medicines and Medical Devices, the List of Essential Medicines, the Program for the Protection of the Population from HIV Infection in the Republic of North Macedonia, as well as others listed further below.

For several aspects covered by the WHO Guidelines, for which no specific recommendations were included in the relevant national documents, an analysis of the existing practice was conducted focusing on the period of the last two years (2018 and 2019) in order to reflect current or most recent practices. In this regard, the consultants considered official documentation for public procurements of ARVs in 2018 and 2019, data from anonymized patient files regarding treatment regimens that patients were taking at the time of the analysis (December 2019) and the initial treatment regimens for patients that started treatment in 2018 and 2019, as well as the time between confirming HIV diagnosis and starting treatment. The annual National HIV Program (Program for the Protection of the Population from HIV Infection) for the period between 2011 and 2019 was also consulted. During the analysis consultants noted that there was a need for a face to face interview with the key HIV clinician and national HIV coordinator in order to be able to assess the actual practice in the country (i.e. at the Clinic for Infectious Diseases) having in mind the lack of specific recommendations in the existing official documents.

WHO recommendations that are formulated to refer specifically to a generalized epidemic or to settings with high burden of HIV and TB were not analyzed because of the significant difference in the context.

Overview of the main documents analyzed

1. The main official document mentioned in the introduction is titled Guidelines for the medical care regarding HIV infection (in Macedonian: Упатство за медицинското згрижување при ХИВ инфекција). The last version of this document was published in 2015 with a Ministerial Decree — No. 17-2490/1 from 27 February 2015. This document is part of a series of guidelines for different disease areas and it is based on the Law on Health Protection, the main legal act regulating health care in the country. This Law mandates that health care is delivered in health institutions by health workers and health collaborators in accordance with expert guidelines for evidence-based medicine, which are established by the minister

of health in accordance with the contemporary global medical practice (article 27, paragraph 1 of the Law on Health Protection). The Guidelines on HIV state that health workers and health collaborators deliver the health protection, as a rule, in accordance with these guidelines (article 3 of the Guidelines). However, by exception, a medical professional is allowed to diverge from the provisions of the Guidelines with an adequate written explanation of the reasons and the need for such divergence (ibid.).

There is no general provision that defines the frequency of revision, but the Guidelines published in 2015 state that subsequent revision was planned to happen in 2016, which has not been the case in practice.

The last version of the Guidelines from 2015 states that it was up-dated by only one doctor — no editorial board is mentioned, apart from a guidelines coordinator.

The document makes references to evidence, but there is no explanation of a specific system that applies. It is noteworthy that some of the evidence and sources referred to had been quite outdated even at the time when the Guidelines were made official (2015). For example, the document makes reference to the WHO Guidelines from 2006 (World Health Organization (WHO) Guidelines. Antiretroviral therapy for HIV infection in adults and adolescents in resource-limited settings: towards universal access: recommendations for a public health approach. June 2006) and the EACS Guidelines of 2008).

Despite the mandatory character of these Guidelines (as described above), the document does not provide a comprehensive and up-to-date guidance for the medical care in relation to the HIV infection, as will be shown further below in the present analysis. Moreover, according to the chief HIV clinician and National HIV Coordinator, there was no consultation process before this document was published by the Ministry of Health in 2015 and even though one infectious diseases specialist was involved in the drafting, no HIV clinician was consulted. According to her, this document is not followed in practice, considering that it is too general and contains a number of outdated references. Instead, the University Clinic for Infectious Diseases and Febrile Conditions (CID) as the only institution that provides treatment and medical care regarding HIV infection refers to the most recent WHO and European AIDS Clinical Society (EACS) Guidelines as guiding documents in the provision of treatment and care to patients.

2. The second document that is meant to provide guidance for professionals in the area of treatment and prevention of HIV is titled Protocol for managing HIV-infected individuals in a general infectology outpatient clinic (in Macedonian: Протокол на работа кај ХИВ-инфицирани лица во општа инфектолошка амбуланта) and is an official internal document of the University Clinic for Infectious Diseases and Febrile Conditions, the only medical institution that provides treatment of HIV in the country. This protocol was made official in 2012 and, as the title suggests, is meant to provide guidance for the doctors working in the general outpatient department of the Clinic.

3. Diagnostic aspects including diagnostic algorithms are part of the Program for ensuring the quality of laboratory testing for HIV in the Republic of Macedonia (Програма за обезбедување на квалитет на лабораториското тестирање на ХИВ во Република Македонија) from 2008, which includes testing algorithms.

4. Guidelines for voluntary counseling and testing for HIV 2011
5. Guidelines for antenatal care 2015 — published by Ministry of Health.

Documents that additionally regulate the use and the supply of ARVs in North Macedonia

Other relevant documents that regulate the use and the provision of antiretroviral medicines specifically include the following:

Program for the Protection of the Population from HIV Infection in the Republic of North Macedonia (Програма за заштита на населението од ХИВ-инфекција во Република Северна Македонија) — published annually by the Ministry of Health — is the national HIV program of the Ministry of Health which covers both treatment and prevention. Since the state took over the financing responsibility for antiretroviral treatment from the Global Fund in 2011, the budget for ARVs has been allocated annually within this national program and based on it the University Clinic for Infectious Diseases and Febrile Conditions is responsible to conduct an annual procurement. The Program does not specify the individual ARVs that are to be procured. The Director of the Clinic and chief HIV clinician confirmed that the decision on the choice of ARVs sits entirely with the Clinic, as the only health institution that offers HIV treatment in the country, noting that the Clinic has to plan the procurement within the available budget. Since 2018 the National HIV Program also includes the financing of the prevention and support services for the key affected populations (men who have sex with men, sex workers, people who inject drugs and people living with HIV) that are delivered by civil society organization (National HIV Program 2018; 2019).

Program for participation in the use of health protection related to specific diseases of the citizens and of health protection of women in labor and newborn babies in the Republic of North Macedonia (Програма за партиципација при користењето на здравствена заштита на одделни заболувања на граѓаните и здравствена заштита на родилките и доенчињата во Република Северна Македонија) — published annually by the Ministry of Health — ensures that the treatment for people with a certain diagnosis from a list defined in this Program, which includes HIV infection, is entirely free of charge. This Program provides funds to cover the amounts of co-payment that patients would normally be required to pay as an out-of-pocket expense.

The List of Medicines Reimbursed by the Health Insurance Fund (Листа на лекови кои паѓаат на товар на Фондот за здравствено осигурување) — defines the medicines which are reimbursed by the state mandatory health insurance. Except for lamivudine, with an indication for acute fulminant hepatitis B and for chronic hepatitis B, no other ARVs are included in the last revision of this list, which was published in 2015 (Official Gazette of RM No. 17 from 05.02.2015). According to the Director of the University Clinic for Infectious Diseases and Febrile Conditions and chief HIV clinician, ARVs have never been procured through the funds of the National Health Insurance Fund, but only with the budget of the National HIV Program (as described above).

List of Essential Medicines (Листа на есенцијални лекови) — The Law on Medicines and Medical Devices defines essential medicines as “basic medicines for the purpose of treating the major part of the population”, “defined as such by a responsible organ” (Article 2). If medicines are listed as essential it constitutes a basis for such products to be issued an importation license, even if they are not registered (Article 79). The prices

of medicines listed in the List of essential medicines, as well as the prices of all prescription medicines, are regulated in accordance with the Law on Medicines and Medical Devices (unlike other medicines which can be priced freely) (107). Prescription medicines and essential medicines can be on the market only after their price has been established in accordance to the Law on Medicines and Medical Devices (Article 107). The List of Essential Medicines is approved by the Minister of Health (ibid.).

The last revision of the List of Essential Medicines was published in 2015 (Official Gazette of RM, No. 19 from 09.02.2015) and it includes the following ARVs: ABC, FTC, 3TC, ZDV, TDF, ddI, d4T, EFV, IDV, LPV/r, NFV, ritonavir. It lists medicines that have not been part of the WHO model lists for several years — and were not part of the WHO Model List of 2015, such as ddI, IDV and NFV. More important, however, is the comparison with the 2019 WHO Model List of EM, which does not include d4T anymore (d4T was excluded already in the 2017 edition of WHO list), but lists several other important medicines, including DTG, RAL, DRV and ATV, as well as a number of fixed-dose combinations, including ABC/3TC, DTG/3TC/TDF, EFV/FTC/TDF, EFV/3TC/TDF, FTC/TDF, 3TC/NVP/ZDV, 3TC/ZDV — all of which are absent in the Macedonian List of 2015.

Part 1. Basic information	
Name of the current version of document.	Guidelines for medical care regarding HIV infection (in Macedonian: "Упатство за медицинското згрижување при ХИВ инфекција") Also relevant: Protocol for work with HIV/infected individuals in a general infectology outpatient clinic (in Macedonian: Протокол на работа кај ХИВ-инфицирани лица во општа инфектолошка амбуланта), not available on-line
Year of the current version.	2015 — Guidelines for medical care regarding HIV infection (Упатство за медицинското згрижување при ХИВ инфекција) 2012 — Protocol for work with HIV/infected individuals in a general infectology outpatient clinic (Протокол на работа кај ХИВ-инфицирани лица во општа инфектолошка амбуланта)
No. of the normative document defining the status of these recommendations (order, resolution, if applicable).	17-2490/1 (27 February 2015) — published in the Official Gazette of the Republic of Macedonia
Legal status of recommendations: mandatory or advisory in nature, what additional documents govern the need for recommendations.	Guidelines are based on the Law on Health Protection and can be considered mandatory by law, despite the fact that the practice does not follow them due to the fact they are outdated
Frequency of the document revision (is it defined? by which documents is it regulated?).	The Guidelines published in 2015 state that subsequent revision was planned to happen in 2016, which has not been the case in practice.
Level of evidence (description of the applicable system).	Levels of evidence are noted, but no system is described.
Members of the editorial board (are representatives of NGOs/patient organizations included?).	The last version of the Guidelines states that it was up-dated by only one doctor — no editorial board is mentioned, apart from a coordinator responsible for the guidelines for all medical specialties.
List and brief description of documents additionally regulating the use of ARVs in the country, including the following documents, but not limited to: · laws governing the nature of supplying the ARVs (free of charge/ paid, by prepaid medical care plan or at the expense of a special national program, etc.); · lists of Vital and Essential Drugs; · lists of drugs to be procured at the expense of different budgets; · treatment standards, etc.	· Program for the Protection of the Population from HIV Infection in the Republic of Macedonia · (Програма за заштита на населението од ХИВ-инфекција во Република Македонија) — published annually by the Ministry of Health. · Program for participation in the use of health protection related to specific diseases of the citizens and of health protection of women in labor and newborn babies in the Republic of Macedonia (Програма за партиципација при користењето на здравствена заштита на одделни заболувања на граѓаните и здравствена заштита на родилките и доенчињата во Република Македонија) — published annually by the Ministry of Health. · List of Medicines Reimbursed by the Health Insurance Fund · (Листа на лекови кои паѓаат на товар на Фондот за здравствено осигурување) — last revision published in 2015 (Official Gazette of RM No. 17 from 05.02.2015) · List of Essential Medicines · (Листа на есенцијални лекови) — last revision published in 2015 (Official Gazette of RM, No. 19 from 09.02.2015)

Page and quote from national protocols	Comment	Link to relevant WHO recommendation, page, document, quote
Part 2. Guidelines for diagnostics		
Retesting before inclusion in care and treatment programs. No specification indicated in both protocols. It is only stated in the MoH Guidelines (page 3) that 'After a first positive HIV test (ELISA or rapid test) the patient is referred to the counselling center and HIV outpatient clinic for further counseling and verification of the HIV positive test'.	As practice at the clinic, if patient is coming at the clinic with HIV positive test, confirmation test is conducted at the clinic and counselling is done by the medical doctor or psychologist.	**WHO 2016, p. 19:** National programs should retest all people newly and previously diagnosed with HIV before they enroll in care and initiate ART. Retesting people on ART is not recommended, as there are potential risks of incorrect diagnosis, particularly for in vitro diagnostics (IVDs) that use oral fluid specimens

Pre-test and post-test advising services. **MoH Guidelines, page 3:** Adequate time must be set in order to communicate the positive result of the test. The patient should be given detailed instructions on how to get more information or moral support (AIDS helplines, support organizations, etc.). If necessary, a specialist in infectious diseases should be consulted prior to meeting the patient. · If the HIV test is negative, advise the patient to reduce risk behavior and, if necessary, repeat the test. · Any institution making and delivering positive HIV test results must be trained to advise the patient on the ways of transmission and prevention of the infection, the development of the disease and the available treatment options for HIV infection. The institution must be prepared to answer the questions related to the daily hygiene needs in the future etc. (B). · Monitoring the patient, determining the stage of the disease, as well as specific treatment further, are provided by a team of specialists in the field. · Find people who have been in risky contact with the patient as quickly and effectively as possible and encourage them to be tested. · Officially reporting an infectious disease is mandatory. · If the patient is an IV drug user, hepatitis B vaccination is recommended if the patient has not had the disease in the past or has been vaccinated. An HCV test should also be done. Patients are further monitored by a team of infectologists. Patients on therapy should be monitored regularly every 3-6 months.	Pre and post-test counselling is conducted at the Clinic. There is no official counseling protocol, although there is existing Guidelines for voluntary counseling and testing at the national level published in 2011, which is intended for use by both public health institutions and civil society organizations where VCT is offered. The Institute of Pulmonary Diseases and Tuberculosis has developed its own working protocol for HIV and TB and counseling.	**WHO, 2016, page 21:** Initiatives should be put in place to enforce privacy protection and institute policy, laws and norms that prevent discrimination and promote the rights of people living with HIV. This can help create environments where disclosure of HIV status is easier (strong recommendation, low-quality evidence).
Testing by non-professional medical workers using express diagnostic methods. There are no specific recommendations in MoH Guidelines and the CID Protocol.	In the country since 2007 there is established community based HIV testing conducted by 14 non-governmental organizations focusing on key populations.	**WHO, 2016, page 27:** Community-based HIV testing services *Generalized HIV epidemic* · WHO recommends community-based HIV testing services with linkage to prevention, treatment and care services, in addition to routinely offering PITC for all populations, particularly key populations (strong recommendation, low-quality evidence). *Concentrated HIV epidemic* · WHO recommends community-based HIV testing services, with linkage to prevention, treatment and care, in addition to PITC for key populations (strong recommendation, low-quality evidence).

Testing initiated by a medical worker.

MoH Guidelines, page 2 and 3:

HIV testing is specifically indicated in the following clinical conditions:

1. History of high-risk behavior: unprotected sexual intercourse with occasional partners or with prostitutes or intravenous drug use.
2. Sexually transmitted diseases.
3. Fever, dementia, or weight loss for no apparent reason.
4. Thrombocytopenia.
5. Tuberculosis in young or middle-aged people.
6. Pneumonia, caused by Pneumocystis jirovecii (Opportunistic pneumonia with typical presentation with slow onset, dyspnoea onset, hypoxemia and mildly elevated or moderate temperature).
7. Oral candidiasis with dysphagia or swallowing pain (esophageal candidiasis).
8. Kaposi's sarcoma (wine-red or purple spots or gum, gum or skin tumor).
9. In a patient diagnosed with Hepatitis B or C who have symptoms and signs that suggest primary HIV infection.
10. Cancer of the cervix, especially if it is diagnosed in a young woman.
11. Diagnosed lymphoma.
12. It is recommended that HIV testing be included in screening and testing of immigrants coming from endemic regions.
13. HIV testing should always be done at the patient's request. The patient should seek consent for an HIV test. If the patient rejects the test, the problems and possible consequences of delayed diagnosis, both for the patient and staff (due to additional investments and prolonged treatment time), possible risk of transmission to other persons, should be further discussed and considered with the patient. During the follow-up period condoms should be used.
14. Pregnant women undergo voluntary screening tests in maternity hospitals

Every patient coming in the outpatient clinic at the Clinic for Infectious Diseases is informed when HIV test is indicated to be done.

PITC is offered in relation to TB services, as well as at the Clinic for Infectious Diseases related to different indications.

WHO, 2016, page 27: Facility-based HIV testing services

Generalized HIV epidemic

- PITC should be offered for all clients and in all services (including services for sexually transmitted infections (STI), viral hepatitis, tuberculosis (TB), children under the age of 5 years, immunization, malnutrition, antenatal care and all services for key populations) as an efficient and effective way to identify people with HIV.

Concentrated HIV epidemic

- PITC should be offered for clients (adults, adolescents and children) in clinical settings who present with symptoms or medical conditions that could indicate HIV infection, including presumed and confirmed TB cases.

Regardless of epidemic type

- PITC should be considered for malnutrition clinics, STI, hepatitis and TB services, ANC settings and health services for key populations.
- For TB settings, routine HIV testing should be offered to all clients with presumptive and diagnosed TB; partners of known HIV-positive TB patients should be offered voluntary HTS with support for mutual disclosure (strong recommendation, low-quality evidence in accordance with the recommendation for the partners of all people living with HIV, and TB control programmes should mainstream provision of HTS in their operations and routine services

Diagnosis of HIV infection in children and infants, in particular, the sensitivity and specificity of tests. There are no specific recommendations in MoH Guidelines and the CID Protocol.	The Clinic for Infectious Diseases as the reference center for HIV diagnosis follows WHO recommendations in this regard.	**WHO, 2016, page 29: HIV diagnosis in infants and children** · It is strongly recommended that HIV serological assays used for the purpose of clinical diagnostic testing have a minimum sensitivity of 99% and specificity of 98% under quality-assured laboratory conditions (strong recommendation, moderate-quality evidence). · It is strongly recommended that HIV virological assays used for the purpose of clinical diagnostic testing (usually at or after 6 weeks of age) have a sensitivity of at least 95% and ideally more than 98%, and specificity of 98% or more under quality-assured, standardized and validated laboratory conditions (strong recommendation, moderate-quality evidence). · It is strongly recommended that HIV virological testing be used to diagnose HIV infection in infants and children below 18 months of age (strong recommendation, high-quality evidence). · In infants and children undergoing virological testing, the following assays (and respective specimen types) are strongly recommended for use: HIV DNA on whole blood specimen or DBS; HIV RNA on plasma or DBS; Us p24Ag on plasma or DBS (strong recommendation, high-quality evidence). · It is strongly recommended that all HIV-exposed infants have HIV virological testing at 4–6 weeks of age or at the earliest opportunity thereafter (strong recommendation, high-quality evidence). · In infants with an initial positive virological test result, it is strongly recommended that ART be started without delay and, at the same time, a second specimen be collected to confirm the initial positive virological test result. Do not delay ART. Immediate initiation of ART saves lives and should not be delayed while waiting for the results of the confirmatory test (strong recommendation, high-quality evidence). · It is strongly recommended that test results from virological testing in infants be returned to the clinic and child/mother/caregiver as soon as possible, but at the very latest within 4 weeks of specimen collection. Positive test results should be fast-tracked to the mother–baby pair as soon as possible to enable prompt initiation of ART (strong recommendation, high-quality evidence). · It is strongly recommended that all infants with unknown or uncertain HIV exposure being seen in health-care facilities at or around birth or at the first postnatal visit (usually 4–6 weeks) or other child health visit have their HIV exposure status ascertained (strong recommendation, high-quality evidence). · It is strongly recommended that HIV-exposed infants who are well undergo HIV serological testing at around 9 months of age (or at the time of the last immunization visit). Infants who have reactive serological assays at 9 months should have a virological test to identify HIV infection and the need for ART (strong recommendation, low-quality evidence).

Testing in special groups (adolescents, pregnant women, couples and partners).

There are no specific recommendations in MoH Guidelines and the CID Protocol.

Guidelines for antenatal care 2015, p. 12:

- Pregnant women should be recommended screening for HIV infection early in the antenatal care, as appropriate antenatal interventions can reduce of the mother-to-child transmission of HIV [snp-A].
- There should be a clear clinical guidance system in each working unit or department for women with this finding and thus pregnant women diagnosed with HIV infection would be guided and treated by appropriate specialist teams [snp-D].

HIV testing services with linkage to prevention, treatment and care are available through civil society organizations, but they are not accessible to adolescents due to legal barriers for providing any kind of medical service without parental consent to people less than 18 years of age.

PITC for women during pregnancy is included in the Guidelines for antenatal care of the MoH from 2015.

There are no specific recommendations at the national level for testing of couples and partners.

WHO 2016, p. 42: Adolescents

HIV testing services, with linkages to prevention, treatment and care, should be offered for adolescents from key populations in all settings (strong recommendation, very low-quality evidence).

- Adolescents with HIV should be counselled about the potential benefits and risks of disclosure of their HIV status, and empowered and supported to determine if, when, how and to whom to disclose (conditional recommendation, very lowquality evidence).

Generalized HIV epidemic

- HIV testing services with linkage to prevention, treatment and care should be offered to all adolescents in generalized epidemics (strong recommendation, very low-quality evidence).

Concentrated HIV epidemic

- HIV testing services with linkage to prevention, treatment and care should be accessible to adolescents in low-level and concentrated epidemics (conditional recommendation, very low-quality evidenc

Pregnant women, page 43:

High-prevalence settings

- PITC for women should be considered a routine component of the package of care in all antenatal, childbirth, postpartum and paediatric care settings. In such settings, where breastfeeding is the norm, lactating mothers who are HIV negative should be retested periodically throughout the period of breastfeeding.
- All HIV-negative pregnant women should be retested in the third trimester, postpartum and/or during labour, because of the high risk of acquiring HIV during pregnancy.

Low-prevalence settings

- PITC can be considered for pregnant women in antenatal care as a key component of the effort: — to eliminate mother-to-child transmission of HIV — to integrate HIV testing with other key testing (for viral hepatitis, syphilis etc.) as relevant to the setting — to retest HIV negative pregnant women who are in a serodiscordant couple, from a key population group or have known ongoing HIV risk.

Couples and partners, page 44:

Couples and partners should be offered voluntary HIV testing services with support for mutual disclosure. This applies also to couples and partners from key populations (strong recommendation, low-quality evidence).

- In antenatal care settings, couples and partners should be offered voluntary HIV testing services with support for mutual disclosure (strong recommendation, low-quality evidence). · HIV testing services for couples and partners, with support for mutual disclosure, should be offered to individuals with known HIV status and their partners (strong recommendation, low-quality evidence for all people with HIV in all epidemic settings; conditional recommendation, low-quality evidence for HIV-negative people depending on the country-specific HIV prevalence).

Key populations Guidelines for voluntary counseling and testing for HIV 2011, p. 14 — 6. VCT AMONG VULNERABLE GROUPS IN REPUBLIC OF MACEDONIA (specifically named: men who have sex with men, people who inject drugs, sex workers, prisoners and youth)	HIV testing services for key affected populations are included in the national Guidelines for voluntary counseling and testing for HIV (2011) and they are in line with WHO recommendations. HTS are offered to KAPs by service-delivery CSOs through the National HIV Program, funded from the state budget starting from 2018.	**Key populations, page 45:** · HIV testing services should be routinely offered to all key populations in the community, in closed settings such as prisons and in facility-based settings. · Community-based HIV testing services for key populations linked to prevention, treatment and care services are recommended, in addition to routine facility-based HIV testing services, in all settings (strong recommendation, low-quality evidence).
Diagnostic algorithms. CID protocol, page 1: Confirmation of an HIV positive test is done with 2 subsequent ELISA tests and 1 Western blot (Western blot with a different blood sample). Program for ensuring the quality of laboratory testing for HIV in the Republic of Macedonia published by the Ministry of Health in 2008 specifies diagnostic algorithms that are still in use by confirmatory laboratories.	According to the diagnostic algorithms that are in use, either Western blot or RT-PCR (depending on the type and result of the previous test) is mandatory for confirming the diagnosis and RDTs are not taken into consideration in the procedure for confirming the diagnosis. According to the National HIV Coordinator there has been a discussion within the National HIV Commission on the need to revise and simplify the diagnostic algorithms in accordance to the recent WHO recommendations.	**WHO 2016, p. 46:** *Low-prevalence settings* · In settings with less than 5% HIV prevalence in the population tested, diagnosis of HIV positive should be provided to people with three sequential reactive tests. — For individuals where the Assay 1 result is reactive and Assay 2 result is non-reactive, the final result should be considered HIV negative. However, in the case of such results and where Assay 1 is a fourth-generation assay (antibody/antigen [Ab/Ag]) and Assay 2 is an Ab-only assay, the result should be considered inconclusive and the person should be retested after 14 days. — For individuals with results in which Assay 1 is reactive, Assay 2 is reactive and Assay 3 is non-reactive, the result should be considered inconclusive and the client should be asked to return in 14 days for retesting. *All settings* · HIV testing services may use combinations of RDTs or combinations of RDTs/ enzyme immunoassays (EIAs)/supplemental assays rather than EIA/Western blot combinations.
Part 3. ARVs for HIV prevention		
Pre-exposure prophylaxis of HIV infection. **MoH 2015, p. 6:** Pre-exposure prophylaxis with oral tenofovir disoproxil fumarate (TDF) alone or with TDF + emtricitabine (FTC) allows reduction of the risk of acquiring HIV in high-risk individuals including people in sero-different relationships, a man having sex with a man and another high risky man and woman (B).	PrEP is not adequately covered in any of the official guidelines/ protocols, although the MoH Guidelines do make only a general mention of PrEP. At the moment of conducting this analysis there is an established working group developing national PrEP guidelines with support by a WHO expert.	**WHO 2016 , page 52:** **Oral pre-exposure prophylaxis for preventing the acquisition of HIV** Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches (strong recommendation, high-quality evidence).

Algorithm and regimens of post-exposure prophylaxis for different population groups, including for PMTCT. MoH 2015, p. 4-5: Prophylactic therapy may significantly reduce the risk of HIV infection after occupational or other incidental exposure (for example, when a condom breaks during sexual intercourse with HIV discordant couples). Prophylactic protection is recommended to be started as early as possible during the first 2 hours but not later than 72 hours after exposure. The nearest center responsible for the treatment of HIV infection should be consulted to decide whether prophylactic therapy should be initiated. Protocol on PEP for accidents among health workers with an HIV-positive patient, p. 1: · Ideally to start with PEP <4 h and not later od 36-72 h · The treatment period is 4 weeks · PEP regimen: TDF/FTC (alternative ZDV/3TC) + LPV/r tablets 400/100 mg or SQV/r 1000/100 mg. · recommended testing of the source (is HIV status in unknown) · if the source is HIV positive and receives ART, genotypisation should be done if HIV RNA is > 1000 copies/microL ARV regimen for PEP (page 2) · recommended treatment with 2 nucleosid analogue inhibitors when: · source HIV status is not know · HIV resistance prevalence in the region is under 15% · source patients has never used ARV · First line ART (ZDV 300 mg+ 3TC 150 mg (2x1) · Alternative regimen: TDF 300 mg 1x1+ 3TC 150 mg (2x1) · Recommended treatment with 3 ART drugs (2 nucleoside analogues inhibitors + boosted protease inhibitor) when: · source is HIV positive patient receiving ART treatment · resistance prevalence in the region is above 15% ART regimen: · first line (ZDV + 3TC plus LPV/r 400/100 mg 2x1) · alternative regimen: ZDV + 3TC or TDF+ 3TC plus ATV/r 300/100 mg 2x1 or SQV/r 1000/100 mg 2x1 or FOS/r 700/100 mg	The MoH Guidelines include only a general recommendation on PEP which mentions both occupational and other incidental exposure and refers to the nearest center responsible for the treatment of HIV infection. However, the specific recommendations on administering PEP are included in the Protocol on post-exposure prophylaxis for accidents among health workers with an HIV-positive patient of the Clinic for Infectious Diseases which covers only occupational exposure. In line with the above, PEP is currently available only for medical workers. The existing recommendations on PEP are more or less in line with WHO 2016 recommendations in terms of the choice of regimen, but not with the 2018 up-date. At the moment established working group is developing a new national post-exposure prophylaxis protocol for both occupational exposure and for sexual exposure.	**Post exposure prophylaxis, WHO 2016, page 61 and 62:** · A regimen for post-exposure prophylaxis for HIV with two ARV drugs is effective, but three drugs are preferred (conditional recommendation, very low-quality evidence). Post-exposure prophylaxis ARV regimens for adults and adolescents: TDF + 3TC (or FTC) is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis for adults and adolescents (strong recommendation, low-quality evidence). LPV/r or ATV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for adults and adolescents (conditional recommendation, very low-quality evidence). Where available, RAL, DRV/r, or EFV can be considered as alternative options. Post-exposure prophylaxis ARV regimens for children ≤10 years: AZT + 3TC is recommended as the preferred backbone regimen for HIV postexposure prophylaxis for children aged 10 years and younger. ABC + 3TC or TDF + 3TC (or FTC) can be considered as alternative regimens (strong recommendation, low-quality evidence). LPV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for children younger than 10 years (conditional recommendation, very low-quality evidence). An age-appropriate alternative regimen can be identified among ATV/r, RAL, DRV, EFV and NVP. Clinical considerations NVP should not be used in children above the age of 2 years. Prescribing practices: A 28-day prescription of antiretroviral drugs should be provided for HIV post-exposure prophylaxis following initial risk assessment (strong recommendation, low-quality evidence). -Enhanced adherence counselling is suggested for individuals initiating HIV post-exposure prophylaxis (conditional recommendation, moderate-quality evidence). **WHO 2018, p. 37:** *Overall* An HIV post-exposure prophylaxis regimen with two ARV drugs is effective, but three drugs are preferred (conditional recommendation, low-certainty evidence) *Adults and adolescents* TDF + 3TC (or FTC) is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis (strong recommendation, low-certainty evidence) DTG is recommended as the preferred third drug for HIV post-exposure prophylaxis (strong recommendation, low-certainty evidence) When available, ATV/r, DRV/r, LPV/r and RAL may be considered as alternative third drug options for post-exposure prophylaxis (conditional recommendation, low-certainty evidence) *Children* AZT + 3TC is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis for children. ABC + 3TC or TDF + 3TC (or FTC) can be considered as alternative regimens (strong recommendation, low-certainty evidence) DTG is recommended as the preferred third drug for HIV post-exposure prophylaxis for children for whom an approved DTG dosing is available (strong recommendation, low-certainty evidence) When available, ATV/r, DRV/r, LPV/r and RAL may be considered as alternative third drug options for post-exposure prophylaxis (conditional recommendation, low-certainty evidence)
Other points not mentioned above.		

Part 4. Antiretroviral therapy regimens		
When ART should be started, including recommendations for specific groups of patients (for whom urgent indication is recommended). The MoH Guidelines of 2015 state on page 4: "Indications for starting treatment in HIV infection are: · Symptomatic disease (in particular in case of an AIDS diagnosis). · Asymptomatic patients if number of CD4 cells has fallen below 0.35x 109/L. · In HIV positive pregnant women (in order to prevent vertical transmission) (evidence level — A)"	The recommendation of the MoH Guidelines is not followed when it comes to the CD4 count threshold. Treatment is offered to all patients regardless of CD4 count in accordance to WHO and EACS guidelines. The recommendation regarding pregnant women coincides with WHO Guidelines of 2016, but it is not as specific. An analysis of the time from the date of diagnosis to the date of ART initiation for the patients diagnosed in 2018 and 2019 (until November) showed a median of 20 days.	**WHO 2016, p. 74:** "ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count (strong recommendation, moderate-quality evidence). As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤350 cells/mm3 (strong recommendation, moderate-quality evidence)." WHO 2016, p. 81: "ART should be initiated in all pregnant and breastfeeding women living with HIV regardless of WHO clinical stage and at any CD4 cell count and continued lifelong (strong recommendation, moderate-quality evidence)."
Adolescents	There is no specific recommendation regarding adolescents in the MoH Guidelines in terms of when to start. The practice is in line with WHO 2016 Guidelines.	**WHO 2016, p. 86:** "ART should be initiated in all adolescents living with HIV, regardless of WHO clinical stage and at any CD4 cell count (conditional recommendation, lowquality evidence). As a priority, ART should be initiated in all adolescents with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adolescents with a CD4 count ≤350 cells/mm3 (strong recommendation, moderate-quality evidence)."
Children	There is no specific recommendation for starting treatment in children. WHO Guidelines are followed in practice.	**WHO 2016, p. 89:** "ART should be initiated in all children living with HIV, regardless of WHO clinical stage or at any CD4 cell count: · Infants diagnosed in the first year of life (strong recommendation, moderatequality evidence); · Children living with HIV 1 year old to less than 10 years old (conditional recommendation, low-quality evidence). As a priority, ART should be initiated in all children ≤2 years of age or children younger than 5 years of age with WHO clinical stage 3 or 4 or CD4 count ≤750 cells/mm^3 or CD4 percentage <25%, and children 5 years of age and older with WHO HIV clinical stage 3 or 4 disease or CD4 count ≤350 cells/mm^3 (strong recommendation, moderate-quality evidence)."
Patients coinfected with TB	There are no specific recommendations in the MoH Guidelines regarding the timing of ART for adults and children with TB. WHO recommendations are followed in practice.	**WHO 2016, p. 93:** "ART should be started in all TB patients living with HIV, regardless of CD4 cell count (strong recommendation, high quality evidence). TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment (strong recommendation, high-quality evidence). HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm3) should receive ART within the first two weeks of initiating TB treatment. ART should be started in any child with active TB disease as soon as possible and within 8 weeks following the initiation of antituberculosis treatment, regardless of the CD4 cell count and clinical stage (strong recommendation, low-quality evidence)."

Choosing the Line 1 drugs	The Guidelines of the Ministry of Health do not give specific recommendations on what regimens to use. They refer to the EACS Guidelines of 2008(!). According to the chief HIV clinician and National HIV Coordinator, in practice the choice of treatment is guided by referring to the most recent EACS guidelines and WHO guidelines. The availability of treatment options in the country influences the choice of treatment, considering that the market is very small and there have been challenges in procuring certain ARVs. If one of the preferred treatment regimens in either EACS or WHO guidelines cannot be followed, then an alternative regimen is used. The use of regimens not listed as preferred on alternative in either WHO or EACS guidelines is normally avoided.	
Choosing the Line 1 drugs · Most widely used regimens · Use of DTG and EFV400 in accordance with the updated recommendations (2018, 2019). · Recommendations for use of dolutegravir in women of childbearing age and pregnant women.	In 2019 (until 15 December), the majority of patients (94%) were started on the following regimens: **- TDF / FTC / EFV 600 mg (56%)** **- TDF / FTC + NVP (18%)** **- TDF / FTC + RAL (11%)** **- TDF / FTC + DTG (9%)** Other combinations were used as initial treatment regimen in isolated cases: TDF / FTC + DRV + r and ABC / 3TC + EFV Of the regimens used, only TDF / FTC + DTG is a preferred regimen according to both WHO 2019 and EACS 2019. It is evident that one ARV — **NVP — is not included anymore in WHO Guidelines (WHO 2018, 2019)** nor in EACS 2019 as part of any preferred or alternative initial treatment regimen. It was still included, however, in the WHO 2016 Guidelines as an alternative option for first-line for adults, pregnant or breastfeeding women, adolescents and children. The use of EFV 600 mg in combination with TDF + 3TC (or FTC) (which more than half of newly diagnosed patients started with in 2019) was still listed as an alternative first line regimen, but has been excluded in the 2019 up-date, with the exception of special circumstances. Instead, WHO is now recommending the use of EFV 400 mg as an alternative first-line regimen. The combination of **TDF / FTC + RAL**, which was used as 1st line in about 10% of patients who started ART in 2019 is only listed for special circumstances in WHO 2019. There is a notable difference in 2019 compared to 2018, when the following regimens were predominant as initial treatment combinations for the majority (97.5%) of people who started ART in that year: **TDF / FTC / EFV 600 mg (32.5%)** **TDF / FTC + NVP (32.5%)** **AZT / 3TC + NVP (17.5%)** **AZT / 3TC + EFV 600 mg (7.5%)** **TDF / FTC + LPV/r (7.5%)** From the above it can be noted that the proportion of patients starting with NVP has decreased significantly between 2018 and 2019, whereas the use of AZT and LPV/r has phased out completely. According to the chief HIV clinician this was based on the EACS Guidelines, which did not include neither of these medicines anymore as part of the recommended regimens.	**WHO 2016, p. 98:** "If TDF + 3TC (or FTC) + EFV is contraindicated or not available, one of the following alternative options is recommended: – AZT + 3TC + EFV – AZT + 3TC + NVP – TDF + 3TC (or FTC) + NVP (strong recommendation, moderate-quality evidence)." **WHO 2019, p. 3:** "First-line ART regimens 1. Dolutegravir (DTG) in combination with a nucleoside reverse-transcriptase inhibitor (NRTI) backbone is recommended as the preferred first-line regimen for people living with HIV initiating ART · Adults and adolescents (strong recommendation, moderate-certainty evidence) · Infants and children with approved DTG dosing (conditional recommendation, low-certainty evidence) 2. Efavirenz at low dose (EFV 400 mg) in combination with an NRTI backbone is recommended as the alternative first-line regimen for adults and adolescents living with HIV initiating ARTc (strong recommendation, moderate certainty evidence) 3. A raltegravir (RAL)-based regimen may be recommended as the alternative first-line regimen for infants and children for whom approved DTG dosing is not available (conditional recommendation, low-certainty evidence) 4. A RAL-based regimen may be recommended as the preferred first-line regimen for neonates (conditional recommendation, very-low-certainty evidence)"

	The use of DTG has increased in the recent few years, but it is still limited primarily due to budget constraints. At the moment of finalizing this analysis 10% of the total number of people on ART were taking DTG-based regimens. However, according to the chief HIV clinician, due to the limited quantities this medicine is used more as part of a switch strategy for treatment-experienced patients due to documented toxicities with other drugs, avoidance of drug-drug interactions, ageing and/or comorbidity etc. It would also be prioritized to construct second-line treatment in case a patient has a demonstrated virological failure.	
Choosing the Line 1 drugs · Preferences for fixed dose combination (FDCs) drugs.	Fixed-dose combinations are preferred whenever possible, as per WHO Guidelines.	**WHO 2016, p. 105:** "Fixed-dose combinations and once-daily regimens are preferred for antiretroviral therapy (strong recommendation, moderate-quality evidence)."
Choosing the Line 1 drugs · Refusal to use stavudine.	Stavudine is not used as per WHO recommendations (2016 and earlier). This was confirmed by the chief HIV clinician as the practice for many years now (and was also evident from procurement documentation). Even though not formulated as a specific recommendation, the MoH Guidelines do make mention of stavudine: "The Combination of nevirapine, lamivudine and stavudine has the same efficacy as the combination of efavirenz, lamividine and stavudine in the treatment of HIV infection and AIDS (level of evidence — B)." (MoH 2015, p. 6) Similarly MoH Guidelines make mention of a combination of ABC/3TC/AZT (under proprietary name Trizivir), even though the use of three NRTIs as a treatment regimen has been outdated for a long time and has been advised against by relevant global guidelines for many years now: "Initial HIV treatment with Trizivir has the same virological effect as the combination of efavirenz, nelfinavir and atazanavir. Trizivir is better tolerated and does not have the unfavorable effect on the lipid profile (level of evidence — B)" (MoH 2015, p. 5)	**WHO 2016, p. 98:** "Countries should discontinue d4T use in first-line regimens because of its well-recognized metabolic toxicities (strong recommendation, moderate-quality evidence)."
Line 1 ART for special patient groups.	The MoH Guidelines do not give any recommendations for special patient groups. WHO recommendations are followed in practice. According to the chief HIV clinician and National HIV Coordinator, in the last 5 years there have been no children diagnosed with HIV. There is only one adolescent among the patients of the Clinic, who was diagnosed as a child, more than 7 years ago and is now taking TDF/FTC/ELV/c, but not as the initial combination. In case new children are diagnosed with HIV, the Clinic maintains stocks of AZT, 3TC and LPV/r oral solutions. In the last 5 years there have been only 2 women living with HIV who became pregnant.	**WHO 2019, p. 3:** "First-line ART regimens 1. Dolutegravir (DTG) in combination with a nucleoside reverse-transcriptase inhibitor (NRTI) backbone is recommended as the preferred first-line regimen for people living with HIV initiating ART · Adults and adolescents (strong recommendation, moderate-certainty evidence) · Infants and children with approved DTG dosing (conditional recommendation, low-certainty evidence) 2. Efavirenz at low dose (EFV 400 mg) in combination with an NRTI backbone is recommended as the alternative first-line regimen for adults and adolescents living with HIV initiating ART (strong recommendation, moderate certainty evidence) 3. A raltegravir (RAL)-based regimen may be recommended as the alternative first-line regimen for infants and children for whom approved DTG dosing is not available (conditional recommendation, low-certainty evidence) 4. A RAL-based regimen may be recommended as the preferred first-line regimen for neonates (conditional recommendation, very-low-certainty evidence)"

Recommendations for breastfeeding of babies.	Women are advised not to breastfeed. AZT is given to the newborn for 28 days as prophylaxis.	**WHO 2016, p. 125:** National or subnational health authorities should decide whether health services will principally counsel and support mothers known to be HIV infected to either breastfeed and receive ARVы interventions or avoid all breastfeeding.
Monitoring before and after starting ART.	The MoH Guidelines do not give any recommendations for monitoring of patients with HIV before and after stating ART.	
Monitoring before and after starting ART · At HIV diagnosis	Monitoring tests at HIV diagnosis is conducted in accordance to WHO recommendation, including as regular practice all the recommended and those listed as desirable: · HIV testing (serology for adults and children 18 months or older; EID for children younger than 18 months); · CD4 cell count; · TB symptom screening; · HBV (HBsAg) serology; · HCV serology; · Cryptococcus antigen if CD4 cell count ≤100 cells/mm3; · Screening for STIs; · Pregnancy test to assess if ART initiation should be prioritized to prevent HIV transmission to the child; · Assessment for major non communicable chronic diseases and comorbidities. In addition to the tests recommended by WHO, every patient is also receives the following tests at diagnosis: liver enzymes (ALT and AST), TB, syphilis, cytomegalovirus, Epstein-Barr virus, toxoplasmosis; HLA-B*5701 for ABC.	**WHO 2016, p. 128:** Table 4.10. Recommended tests for HIV screening and monitoring and approaches to screening for coinfections and noncommunicable diseases.
Monitoring before and after starting ART · Follow up before ART	Instead of WHO recommendation for CD4 cell count at every 6–12 months in case ART initiation is delayed, such patients are monitored more frequently for both CD4 cell count and viral load, i.e. at every 4 months.	**WHO 2016, p. 128:** Table 4.10. Recommended tests for HIV screening and monitoring and approaches to screening for coinfections and noncommunicable diseases.
Monitoring before and after starting ART · ART initiation	WHO recommendations are followed with some notes: · Haemoglobin test is done regularly during monitoring visits despite the fact AZT is not used anymore; · Pregnancy test is done only if indicated after assessment; · Alanine aminotransferase is tested regularly at monitoring visits in all patients, regardless of the use of NVP; · Blood pressure measurement; · Serum creatinine and eGFR at starting TDF; · Baseline CD4 cell count. In addition, HLA-B*5701 for ABC is done if it was not done at diagnosis.	**WHO 2016, p. 128:** Table 4.10. Recommended tests for HIV screening and monitoring and approaches to screening for coinfections and noncommunicable diseases.
Monitoring before and after starting ART · Receiving ART	WHO recommendations are followed with some notes: · HIV viral load and CD4 cell count are performed one month after initiating ART and then every four months until the patient has become stable on ART. In patients who are stable they are done every 6 months; · Serum creatinine and eGFR for TDF; · Pregnancy test — if indicated after assessment.	**WHO 2016, p. 128:** Table 4.10. Recommended tests for HIV screening and monitoring and approaches to screening for coinfections and noncommunicable diseases.

Monitoring before and after starting ART • Suspected treatment failure	WHO recommendations are followed with some notes: • Serum creatinine and eGFR for TDF; • Pregnancy test, especially for women of childbearing age not receiving family planning and on treatment with DTG or low-dose EFV; • HBV (HBsAg) serology (if the result was previously negative and the patient was not vaccinated thereafter).	Table 4.10. Recommended tests for HIV screening and monitoring and approaches to screening for coinfections and noncommunicable diseases.
Monitoring before and after starting ART • Routine viral load monitoring	Viral load monitoring is carried out routinely every four months in patients who have not started ART and during the first year after starting treatment. In patients that are stable on ART viral load is monitored every 6 months, along with the CD4 cell count.	**WHO 2016, p.129:** "- Routine viral load monitoring can be carried out at 6 months, at 12 months and then every 12 months thereafter if the patient is stable on ART to synchronize with routine monitoring and evaluation reporting (conditional recommendation, very low-quality evidence). In settings where routine viral load monitoring is available, CD4 cell count monitoring can be stopped in individuals who are stable on ART and virally suppressed (conditional recommendation, low-quality evidence)".
Monitoring before and after starting ART • Virological failure	In practice, viral load is used as the approach to diagnose and confirm treatment failure. The EACS Guidelines definition — not WHO definition — is used in practice for virological failure.	**WHO 2016, p.129:** "Viral load is recommended as the preferred monitoring approach to diagnose and confirm treatment failure (strong recommendation, low-quality evidence). If viral load is not routinely available, CD4 count and clinical monitoring should be used to diagnose treatment failure (strong recommendation, moderate-quality evidence). Viral failure is defined by a persistently detectable viral load exceeding 1000 copies/mL (that is, two consecutive viral load measurements within a 3-month interval with adherence support between measurements) after at least 6 months of starting a new ART regimen. Dried blood spot specimens using venous or capillary whole blood can be used to determine the HIV viral load. A threshold of 1000 copies/mL can be used to determine viral failure when using dried blood spot samples, as defined for testing in plasma (conditional recommendation, low-quality evidence)". **EACS 2019, p.16:** "Incomplete Suppression: HIV-VL > 200 copies/mL at 6 months after starting therapy in PLWH not previously on ART. Rebound: confirmed HIV-VL > 50 copies/mL in PLWH with previously undetectable HIV-VL"

Recommendations for switching to Line 2 ART regimens, including for special patient groups, including the preferred alternative regimen.	The MoH Guidelines do not provide recommendations on switching to Line 2 regimens. According to chief HIV clinician most recent WHO and EACS Guidelines would be followed. In practice either TDF + FTC or ABC + 3TC are used as the two NRTI backbone combinations, which is in line with EACS Guidelines. AZT is not being prescribed anymore. At the beginning of December 2019, the distribution of the available ART regimens for 95% of the patients was as follows: TDF + FTC + EFV 600mg (47%) TDF + FTC + NVP (15%) TDF + FTC + DRV + r (9%) TDF + FTC + RAL (6%) TDF + FTC + DTG (3.5%) TDF + FTC + RPV (2%) ABC + 3TC + DTG (7%) ABC + 3TC + NVP (3%) ABC + 3TC + EFV (2.5%) Other combinations used in a very small number of patients were: TDF + FTC + ATV + r TDF + 3TC + DRV + r ABC + 3TC + RAL ABC + 3TC + DRV + r TAF + FTC + DRV + r TAF + FTC + NVP ZDV + 3TC + DRV + r The available regimens show that the Clinic in Skopje is able to follow current WHO recommendations. According to the chief HIV clinician, so far, the Clinic has faced very few cases of virological failure and they are be able to construct an optimal second-line regimen in such cases in accordance to WHO or EACS recommendations. Also, considering that the total number of patients in carries very low (it was around 300 in December 2019), the Clinic's strategy has been to procure a variety of ARVs for the current patients, so that there is sufficient choice to construct a line-2 or line-3 regimens in case they have patients with virological failure or to be able to switch patients in case of side effects.	**WHO 2018, p. 33:** DTG in combination with an optimized nucleoside reverse-transcriptase inhibitor backbone is recommended as the preferred second-line regimen for people living with HIV for whom non-DTG based regimens are failing. (conditional recommendation, moderate-certainty evidence) DTG in combination with an optimized nucleoside reverse-transcriptase inhibitor backbone is recommended as the preferred second-line regimen for children with approved DTG dosing for whom non-DTG-based regimens are failing. (conditional recommendation, low-certainty evidence) **EACS 10.0 2019, p. 16:** In case of demonstrated resistance mutations - General recommendations: Use at least 2 and preferably 3 active drugs in the new regimen (including active drugs from previously use classes) based on resistance mutations present in current and earlier genotypic analyses. Any regimen should use at least 1 fully active PI/b (e.g. DRV/r) plus 1 drug from a class not used previously e.g. INSTI, FI, or CCR5 antagonist (if tropism test shows R5 virus only), or 1 NNRTI (e.g. ETV), assessed by genotypic testing. Alternatively, a regimen can be constructed with DTG (when fully active) plus 2 NRTIs, of which at least 1 NRTI is fully active.
Recommendations for Line 3 ARVs.	The MoH Guidelines do not provide and recommendations on switching to Line 3 regimens. According to the chief HIV clinician, so far no patients have faced virological failure for the second time. If this happens, WHO and/or EACS recommendations would be followed with the intention to construct a regimen with three active drugs.	**WHO 2016, p.159:** National programmes should develop policies for third-line ART (conditional recommendation, low-quality evidence). · Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as INSTIs and second-generation NNRTIs and PIs (conditional recommendation, low-quality evidence). · Patients on a failing second-line regimen with no new ARV drug options should continue with a tolerated regimen (conditional recommendation, very low quality evidence).

Barriers to accessing key drugs recommended by WHO, when they are available (e.g., no registration, no inclusion in the list of Vital and Essential Drugs or procurement lists, high price, etc.)	Due to the low number of patients, most ARV products that have been used in treating patients in North Macedonia were not registered. In the last two year there has been a trend of registering several ARVs — those that are newer and those that are most used. Out of 17 individual ARV formulations (both standalone and fixed-dose combinations) that were included in the 2019 annual procurement of the Clinic for Infectious Diseases, there were registered products for only 8: **NOT registered:** EFV 600 mg NVP 200 mg Ritonavir 100 mg RAL 400 mg ATV 300 mg TAF/FTC (25 mg + 200 mg) TAF/FTC/ETG/r (10 mg + 200 mg + 150 mg + 150 mg) AZT (pediatric solution) 3TC (pediatric solution) **Registered:** DRV 800 mg TDF 300 mg DTG 50 mg TD(F)/FTC (245 mg + 200 mg) TD(F)/FTC/EFV (245 mg + 200 mg + 600 mg) TD(F)/FTC/RPV (245 mg + 200 mg + 25 mg) ABC/3TC/DTG (600 mg + 300 mg + 50 mg) ABC/3TC (600 mg + 300 mg) Not registered products are procured with an ad-hoc importation license issued by the Agency of Medicines on a case-by-case basis. However, the fact that about half of the ARVs in use are not registered makes the outcomes of procurements uncertain.	N/A
Other points not mentioned above.		

Part 5. Prevention and treatment of co-infections and co-morbidities

Recommendations for the prevention and treatment of co-infections **HIV/Viral Hepatitis C (HCV)** **MoH protocol:** In the paragraph for indication is stated that HIV test is indicated in all HBV and HCV patients with symptoms or signs that might suggest HIV infection (page 3); **CID protocol:** initial screening for HBV and HCV is conducted.	**HIV/Viral Hepatitis C (HCV)** Except for the initial screening for HBV/HCV in both MoH Guidelines and CID Protocol, no other specifications about prevention and treatment are included. The National HIV Coordinator and chief HIV clinician stated that when it comes to HBV and HCV infection the clinic is following WHO and EACS protocols; there have been very few HIV patients co-infected with HBV and even fewer coinfected with HCV (the few patients with HCV coinfection were treated and cured 2 years ago).	**HIV/Viral Hepatitis C (HCV)** **WHO 2016, p. 209:** In general, clinical stabilization of HIV disease with ART is advisable prior to starting treatment for HCV, especially in people with advanced immunosuppression (CD4 count below 200 cells/mm3). The decision to start ART among people coinfected with HCV should follow the same principles as in HIV mono infection. For most HIV/HCV coinfected people, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury.

HIV/HBV **MoH Guidelines 2015** - In the paragraph for indication is stated that HIV test is indicated in all HBV and HCV patients with symptoms or signs that might suggest HIV infection (page 3); **CID protocol:** initial screening for HBV and HCV is conducted.	**HIV/ HBV** Except the initial screening for HBV/HCV in both protocols, no other specifications about prevention and treatment are included. The HIV country coordinator and Chief of the clinic stated that when it comes to HBV and HCV infection the clinic is following WHO and EACS protocols. Total number of around 13 patients are coinfected with HBV. No HCV coinfection is noted.	**HIV/ HBV** **WHO 2016, p. 208/09:** The 2013 WHO Consolidated guidelines on the use of antiretroviral drugs recommended providing ART to all people coinfected with HIV and HBV regardless of CD4 count for those with evidence of severe chronic liver disease. This recommendation has now been superseded by the new recommendation in 2015 to treat all people with HIV regardless of CD4 cell count. Nevertheless, in settings where prioritization is required, people coinfected with HIV and HBV and evidence of severe chronic liver disease should be considered a priority for ART. WHO recommends that adults, adolescents and children with chronic hepatitis B and clinical evidence of cirrhosis (or cirrhosis based on the non-invasive APRI test score >2 in adults) should be treated regardless of alanine aminotransferase (ALT) levels, hepatitis B e antigen (HBeAg) status or HBV DNA levels. The risk of HBV infection may be higher in HIV-infected adults. All people newly diagnosed with HIV should therefore be screened for hepatitis B surface antigen (HBsAg) and vaccinated if non-immune.
HIV/TB **MoH Guidelines, p. 2:** At the paragraph Indications for HIV test it is stated, page 2: tuberculosis in young people or middle aged people; **CID Protocol:** At the primary check-up of diagnosed patients, page 1 is stated: screening for TB: Chest X-ray and TB skin test with CD4 count > 400 mm3. Important CD4 cut offs: any CD4 count pulmonary TB, CD4 less than 100/mm3 miliary and extrapulmonary TB (page1); · sputum collection and sputum culture (page 2). · Opportunistic infections diagnosis/TB diagnosis page 4: sputum, Bronchoalveolar lavage (BAL), liquor and other biological specimen are tested with AFV and QuantiFERON- TB Gold. · Treatment of opportunistic infections for pulmonary and extrapulmonary TB is stated: see TB treatment, page 5 · at the paragraph for Opportunistic infections prophylaxis (page 6) is stated that indication is TB skin test of > or equal of 5 mm or recent contact with acute ill TB person and treatment is based on Isoniazid 300 mg+ Pyridoxin 50 mg once daily in a period of 6 months.	**HIV/TB** No recommendations for prevention and treatment for TB are included in the Ministry of Health Guidelines. Poor info for TB screening and prophylaxis is included in the CID Protocol. The Clinic is following EACS and WHO recommendations. In practice, patients are screened for both active and latent TB using sputum and blood with NAAT. Patients with latent TB are offered IPT for 6 to 9 months.	**HIV/TB** TB diagnosis and treatment, WHO 2016, p. 197: · Xpert MTB/RIF should be used rather than conventional microscopy, culture and drug susceptibility testing (DST) as the initial diagnostic test in adults and children suspected of having multidrug-resistant TB (MDR-TB) or HIV-associated TB (strong recommendation, adults: high-quality evidence; children: very low-quality evidence). · Xpert MTB/RIF should be used in preference to conventional microscopy and culture as the initial diagnostic test for cerebrospinal fluid specimens from patients suspected of having TB meningitis (strong recommendation, very low-quality evidence). · Xpert MTB/RIF may be used as a replacement test for usual practice (including conventional microscopy, culture or histopathology) for testing specific non-respiratory specimens (lymph nodes and other tissues) from patients suspected of having extrapulmonary TB (conditional recommendation, very low-quality evidence). · Except as specifically described below for people with HIV infection with low CD4 counts or who are seriously ill, a urine lateral flow (LF)-LAM should not be used for the diagnosis of TB (strong recommendation, low-quality evidence). · LF-LAM may be used to assist in the diagnosis of active TB in adult inpatients living with HIV, with signs and symptoms of TB (pulmonary and/or extrapulmonary), who have a CD4 count less than or equal to 100 cells/mm3, or people living with HIV who are seriously ill,a regardless of CD4 cell count or with unknown CD4 cell count (conditional recommendation, low-quality evidence). · LF-LAM should not be used as a screening test for active TB (strong recommendation, low-quality evidence).

Isoniazid preventive therapy (IPT), WHO 2016, page 201

Adults and adolescents living with HIV should be screened with a clinical algorithm; those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT (strong recommendation, moderate-quality evidence).

- Adults and adolescents living with HIV who have an unknown or positive tuberculin skin test (TST) status and are unlikely to have active TB should receive at least six months of IPT as part of a comprehensive package of HIV care. IPT should be given to such individuals regardless of the degree of immunosuppression, and also to those on ART, those who have previously been treated for TB and pregnant women (strong recommendation, high-quality evidence).
- Adults and adolescents living with HIV who have an unknown or positive TST status and among whom active TB disease has been safely ruled out should receive at least 36 months of IPT. IPT should be given to such individuals regardless of whether or not they are receiving ART. IPT should also be given irrespective of the degree of immunosuppression, history of previous TB treatment and pregnancy (conditional recommendation, moderate-quality evidence).
- Children living with HIV who do not have poor weight gain, fever or current cough are unlikely to have active TB. Children living with HIV who have poor weight gain, fever or current cough or contact history with a TB case may have TB and should be evaluated for TB and other conditions. If the evaluation shows no TB, they should be offered IPT regardless of their age (strong recommendation, low-quality evidence).
- Children living with HIV who are more than 12 months of age and who are unlikely to have active TB on symptom-based screening and have no contact with a TB case should receive six months of IPT (10 mg/kg/day) as part of a comprehensive package of HIV prevention and care (strong recommendation, moderate-quality evidence).
- In children living with HIV who are less than 12 months of age, only those who have contact with a TB case and who are evaluated for TB (using investigations) should receive six months of IPT if the evaluation shows no TB disease (strong recommendation, low-quality evidence).
- All children living with HIV, after successful completion of treatment for TB, should receive IPT for an additional six months (conditional recommendation, low-quality evidence).

Multidrug-resistant TB and HIV, WHO 2016, page 203:

- Antiretroviral therapy is recommended for all patients with HIV and drug resistant TB requiring second-line antituberculosis drugs irrespective of CD4 cell count, as early as possible (within the first eight weeks) following initiation of antituberculosis treatment (strong recommendation, very low-quality evidence).

Prevention and treatment of relevant noncommunicable diseases: · Cardiovascular diseases; · Depression; · Diseases of the central nervous system; · Kidney diseases; · Substance use. **MoH Protocol, page 7 covers paragraph on other therapy, support in the part of psychotherapy and rehabilitation says:** · Massage therapy, in combination with other stress management modalities, can improve the quality of life of people with HIV / AIDS compared to massage or other stand-alone modalities of therapy (C-C). · Aerobic exercise is safe and people with HIV / AIDS can benefit from it (C).	The clinic is following EACS and WHO recommendations. For every HIV patient regular creatinine serum level is conducted as part of the broad biochemical laboratory analysis. At the clinic psycho-social support and counseling as part of the HIV care is established. If needed, patients are referred to the Psychiatry clinic. For all patient vitamin D checkup is done. There is already established good collaboration with University Clinic for Dermatology and Clinic for Urology, although better practice should be made with Clinic of Cardiology when it comes to CVD management of CVD of elderly patients.	**Assessment and management of cardiovascular diseases, WHO, 2016, page 216:** Assessment and management of cardiovascular risk should be provided for all individuals living with HIV according to standard protocols recommended for the general population (conditional recommendation, very low-quality evidence) • **Good practice statement** Strategies for the prevention and risk reduction of cardiovascular diseases by addressing modifiable factors such as high blood pressure, smoking, obesity, unhealthy diet and lack of physical activity should be applied to all people living with HIV. • **Assessment and management of depression in people living with HIV, page 2019, WHO 2016** Assessment and management of depression should be included in the package of HIV care services for all individuals living with HIV (conditional recommendation, very low-quality evidence). • **Drug use and drug use disorders, WHO 2016, page 221** WHO, the United Nations Office on Drugs and Crime (UNODC) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) recommend a comprehensive package of nine interventions for HIV prevention, treatment and care for people who inject drugs; these are needle and syringe programmes, OST, HIV testing and counselling, ART, preventing and treating STIs, condom programmes, targeted behaviour change communication, preventing and treating viral hepatitis and preventing, diagnosing and treating TB. • **Nutritional care and support, WHO 2016 221/222** · Nutritional assessment (anthropometry, clinical and dietary assessment), counselling and support should be an integral component of HIV care and conducted at enrolment in care and monitored across the care continuum. · WHO is revising recommendations for nutritional care and support of adolescents and adults living with HIV, including pregnant and lactating women. · The 2009 guidelines for an integrated approach to the nutritional care of children living with HIV provide details of nutritional interventions.
Other points not mentioned above.		

Part 6. Provision of health services		
The provision of health services, including but not limited to: · Recommendations for decentralization of services. · Recommendations for redistribution and delegation of services. · Recommendations for integration of services.	The MoH Guidelines do not include any specific recommendations on how treatment and care services should be provided. In North Macedonia there is only one clinical center providing treatment and care to patients with HIV. The distribution (dispensing) of ART is also centralized and done only at the Clinic for Infectious Diseases in Skopje. The Clinic for Infectious Diseases features a separate HIV Department and a Day Center for outpatient care, including dispensing ARVs and providing psychosocial support. The Center offers linkage to civil society organizations for peer support services, as well as for harm reduction and some sexual and reproductive health services that are available through CSOs. There is linkage to community-based support service for visiting the clinic targeting socially disadvantage people living with HIV, as well as distribution of ARVs through courier service for patients who live outside of the capital city.	
	A package of support services in North Macedonia is available at the HIV Day Centre within the Clinic for Infectious Diseases and through service-delivery civil society organizations. The HIV Day Centre offers services from a social worker and a psychologist, including case management, support for HIV disclosure, patient tracing. Peer support and navigation for linkage is available through CSOs, including community-based organizations. Rates of linkage after diagnoses are reported to be very high.	**WHO 2016, p.243:** Following an HIV diagnosis, a package of support interventions should be offered to ensure timely linkage to care for all people living with HIV (strong recommendation, moderate-quality evidence). The following interventions have demonstrated benefit in improving linkage to care following an HIV diagnosis: · streamlined interventions to reduce time between diagnosis and engagement in care, including (i) enhanced linkage with case management, (ii) support for HIV disclosure, (iii) patient tracing, (iv) training staff to provide multiple services and (v) streamlined services (moderate-quality evidence); · peer support and navigation approaches for linkage (moderate-quality evidence); and · quality improvement approaches using data to improve linkage (low-quality evidence).
	CD4 cell count is performed at the HIV Day Centre and the HIV Department for hospitalized patients (both at the Clinic for Infectious Diseases) and results are normally ready within 24 hours. In any case, ART is offered upon diagnoses to all patients with HIV.	**WHO 2016, p. 248:** "CD4 cell count testing at the point of care can be used to prioritize patients for urgent linkage to care and ART initiation (conditional recommendation, low-quality evidence)".
Laboratory connectivity	An electronic system is used in the entire public health care system for communication between health institutions (including laboratories) regarding referrals and test results.	**WHO 2016, p. 249:** "Electronic communication can be considered to transfer test results and reduce delays in acting on the results of early infant diagnosis and other essential laboratory tests (conditional recommendation, low-quality evidence)".

Retention in care	Community-based support is provided for in the National HIV Program (i.e. Program for the Protection of the Population from HIV Infection in the Republic of North Macedonia). Community support services are provided by one community-based organization of people living with HIV and they include peer counselling, peer support for adherence, self-help groups, psychosocial support and financial support for travel costs for people with HIV living in particularly difficult social circumstances.	**WHO 2016, p. 251:** "Programmes should provide community support for people living with HIV to improve retention in HIV care (strong recommendation, low-quality evidence). The following community-level interventions have demonstrated benefit in improving retention in care: · package of community-based interventions (children: low-quality evidence; adults: very low-quality evidence); · adherence clubs (moderate-quality evidence); · extra care for high-risk people (very low-quality evidence)".
Adherence	Adherence support interventions are part of the service packages at the HIV Centre of the Clinic for Infectious Diseases and of community-based support, including peer counsellors, cognitive-behavioral therapy, behavioral skills training and medication adherence training (mobile phone text messages and reminder devices are not part of any package). Fixed-dose combinations are prioritized whenever possible according to the chief HIV clinician and an analysis of the treatment combinations of that patients were taking at the beginning of December 2019, showed that 56% of them were taking a single-tablet regimen, while all other patients are taking at least the 2 backbone medicines as a fixed-dose combination.	**WHO 2016, p. 255:** "Adherence support interventions should be provided to people on ART (strong recommendation, moderate-quality evidence). The following interventions have demonstrated benefit in improving adherence and viral suppression: · peer counsellors (moderate-quality evidence); · mobile phone text messages (moderate-quality evidence); · reminder devices (moderate-quality evidence); · cognitive-behavioral therapy (moderate-quality evidence); · behavioral skills training and medication adherence training (moderate-quality evidence); · fixed-dose combinations and once-daily regimens (moderate-quality evidence)".
Frequency of clinical visits and medication pick-up	In practice, patients who are stable on ART are instructed to show up for a monitoring visit every 6 months, while medication pick-up is normally done for 2 months and, by exception, for 3 or longer — decided on a case-by-case basis.	**WHO 2016, p. 259:** · Less frequent clinical visits (3–6 months) are recommended for people stable on ART (strong recommendation, moderate-quality evidence). · Less frequent medication pickup (3–6 months) is recommended for people stable on ART (strong recommendation, low-quality evidence).
Task shifting and task sharing	It is an established common practice at the HIV Center for trained lay providers (social worker and psychologist) to distribute ART to patients and these providers are staff of the HIV Centre, i.e. the Clinic for Infectious Diseases. Likewise, train non-physician clinicians / nurses can maintain ART. There is no established practice for trained community health workers to dispense ART between regular clinical visits, although unofficially they can facilitate the access to ARVs, by doing the medication pick-up on behalf of patients.	**WHO 2016, p. 262:** Trained and supervised lay providers can distribute ART to adults, adolescents and children living with HIV (strong recommendation, low-quality evidence). · Trained non-physician clinicians, midwives and nurses can initiate first-line ART (strong recommendation, moderate-quality evidence). · Trained non-physician clinicians, midwives and nurses can maintain ART (strong recommendation, moderate-quality evidence). · Trained and supervised community health workers can dispense ART between regular clinical visits (strong recommendation, moderate-quality evidence). These recommendations apply to all adults, adolescents and children living with HIV.

Taking blood finger-prick by non-laboratory staff	This is not practiced at the Clinic for Infectious Diseases nor anywhere else. It has only been discussed so far in relation to HIV testing with rapid diagnostic tests.	**WHO 2016, p. 264:** Good practice statement: Trained and supervised non-laboratory staff, including laypeople, can undertake blood finger-prick for sample collection.
Decentralization	While decentralization is considered to be potentially good for simplifying the treatment and care for people living with HIV in North Macedonia, there are no indications that it could improve access to and retention in care within the local context.	**WHO 2016, p. 266:** Decentralization of HIV treatment and care should be considered as a way to increase access to and improve retention in care: · initiation of ART in hospitals with maintenance of ART in peripheral health facilities (strong recommendation, low-quality evidence); · initiation and maintenance of ART in peripheral health facilities (strong recommendation, low-quality evidence); and · initiation of ART at peripheral health facilities with maintenance at the community level (strong recommendation, moderate-quality evidence).
	Due to the nature of the epidemic, which is considered to be concentrated only among men who have sex with men, with no new cases registered with injecting drug use as the mode of transmission in the last 10 years and more, this recommendation is not considered relevant to the context.	**WHO 2016, p. 270:** ART should be initiated and maintained in eligible people living with HIV at care settings where opioid substitution therapy (OST) is provided (strong recommendation, very low-quality evidence).
STI and family planning services in HIV care settings	There are no specific recommendations on integrating STI and family planning services within HIV care and such integration is not the case in practice with the exception of screening for some STIs (i.e. syphilis) and some elements of family-planning services. According to the National HIV Coordinator and chief HIV clinician, a discussion on this aspect is on-going at the level of the National HIV Commission, with an intention to move things into the direction of integration as per this WHO recommendation.	**WHO 2016, p. 271:** Sexually transmitted infection (STI) and family planning services can be integrated within HIV care settings (conditional recommendation, very low-quality evidence).
	No specific recommendations exist regarding adolescent-friendly HIV services. According to official epidemiological reports, no new cases have been reported among adolescents. According to the chief HIV clinician the existing care and support services at the HIV Centre have been able to satisfy the basic WHO recommendations for the extremely few adolescent patients that the Clinic has had in the last 10 years.	**WHO 2016, p. 274:** Adolescent-friendly health services should be implemented in HIV services to ensure engagement and improved outcomes (strong recommendation, low-quality evidence). · Community-based approaches can improve treatment adherence and retention in care of adolescents living with HIV (conditional recommendation, very low-quality evidence). · Training of health-care workers can contribute to treatment adherence and improvement in retention in care of adolescents living with HIV (conditional recommendation, very low-quality evidence). · Adolescents should be counselled about the potential benefits and risks of disclosure of their HIV status to others and empowered and supported to determine if, when, how and to whom to disclose (conditional recommendation, very low-quality evidence).

Moldova

Part 1. Basic information	
Name of the current version of the document and the link to it.	National Guidelines for Laboratory Diagnosis of HIV Infection National Clinical Protocol No. 211 “HIV infection in adults and adolescents” National Clinical Protocol No. 315 “HIV infection in children 0-10 years old” National Clinical Protocol No. 316 “Prevention of mother-to-child transmission of HIV” National Clinical Protocol No. 314 “Post-exposure prophylaxis of HIV infection” National Clinical Protocol No. 313 “Pre-exposure prophylaxis of HIV infection”
Year of the current edition	2018
The normative document number and its status (order, resolution, if applicable).	Order of the MHLSP No. 409, dated March 16, 2018, On the approval of the National Guidelines for Laboratory Diagnostics of HIV Infection “Order of the MHLSP No. 163, dated February 7, 2018, On the approval of the NCP “HIV infection in adults and adolescents" Order of the MHLSP, No. 165, dated February 7, 2018 Order of the MHLSP, No. 166, dated February 7, 2018 Order of the MHLSP, No. 164, dated February 7, 2018 Order of the MHLSP, No. 162, dated February 7, 2018
Legal status of recommendations: mandatory or advisory (What additional documents govern the need for recommendations).	The status of recommendations prescribed in normative acts, such as the National Guidelines and the National Clinical Protocol (NCP), is regulated by Paragraph 3, Annex 2 “Model-structure of the National Clinical Protocol”, Order No. 124 of March 21, 2008, on the development and approval of National Clinical Protocols: “...NCPs include mandatory and advisory requirements. Mandatory requirements will be met obligatory and included in the institutional clinical protocols”.
Frequency of the document revision (Is it defined? What documents regulate this?).	The frequency of NCP revision is defined in the protocol: usually 2-4 years, but maybe more frequent if necessary.
Level of evidence (description of the applicable system).	One of the mandatory components of the first part of the NCP is the chapter: Argumentation of the evidence base.
Members of the editorial board (Are representatives of NGOs/patient organizations included?).	According to the Order of the MHLSP, No. 124, dated March 21, 2008, On the process of developing and approving National Clinical Protocols: Clause 2.2. The NCPs will be developed based on the most modern international recommendations for diagnosis and treatment based on evidence-based medicine, by interdisciplinary teams of specialists created by the MHLSP directly for each specific field of medicine, in accordance with the approved requirements. This interdisciplinary group, created by the MHLSP to revise or write this protocol, within 2-3 months should develop a draft document, in accordance with Annex 2 “Model-structure of the National Clinical Protocol”, Order of the MHLSP No. 124, dated March 21, 2008, On the process of developing and approving National Clinical Protocols. A multidisciplinary group of authors can include representatives from both the medical community and non-governmental/patient organizations. Further, the draft NCP, according to the order of the MHLSP, No. 349/d, dated September 25, 2012, must be endorsed by the Commission of Experts in the field of clinical pharmacology; laboratory medicine; family medicine; emergency medicine; physical medicine and rehabilitation, other specialists (if necessary), Medicines and Medical Devices Agency; National Health Insurance Company, National Council for Healthcare Accreditation. The NCP data on HIV infection as well as the National HIV Testing Guidelines were discussed at a three-day working meeting with representatives from WHO, UNAIDS, UNICEF, all levels of the medical service, external experts in the field of HIV, as well as civil society.
List and a brief description of documents that additionally regulate the use of ARVs in the country	Law of the Republic of Moldova No. 1409, dated 17 December 1997, “On Medicinal Products” with subsequent amendments. The purpose of this law is to ensure national-level access of the population through the drug supply system to high-quality, effective and harmless drugs while maintaining affordable prices for them, preventing the uncontrolled use of drugs. This law applies in all spheres of activity that deal with drugs: their research, registration, production, implementation in practice, application, import, export, storage, distribution, dispensing, and control. The list of essential drugs was last revised in 2011; revision is scheduled for early 2020.

Part 2. Diagnostic recommendations

The **National Guidelines for Laboratory Diagnosis of HIV Infection** is based on the Consolidated Guidelines for HIV Testing Services published by the WHO in July 2015. The Guidelines is a normative act intended for specialists working in the field of HIV diagnosis, sentinel surveillance, as well as from non-governmental organizations that provide HIV testing services to key populations. The main objectives of these guidelines were to maximize access to HIV testing for earlier detection and to speed up the process of confirming HIV infection as much as possible to initiate ART early.

	Recommendations of national protocols and guidelines	WHO recommendations
Screening for HIV infection	To expand access to HIV testing for screening, it is recommended to use rapid HIV tests at all levels of health care and in the non-governmental sector. *"... Screening for HIV infection is carried out by rapid tests, preferably III and IV generations. Rapid tests increase access to HIV testing among the general population and mostly among hard-to-reach populations (for example, PWID, CSW, MSM) or the population in geographically remote areas..."*	Consolidated Guidelines on HIV Testing Services, Chapter 7 "Making the Diagnosis of HIV Infection" *"...Rapid diagnostic tests (RDTs) are a critical tool for scaling up HIV testing services.* *They can be performed by trained lay providers, health-care workers, and laboratory* *professionals in various settings, irrespective of the infrastructure, as they do not require* *specialized equipment or specimen collection by venepuncture..."*
Retesting before inclusion in care and treatment programs.	The National Guidelines for Laboratory Diagnosis of HIV Infection does not recommend retesting before the inclusion in treatment and care programs since the algorithm for confirming HIV infection itself differs from the one recommended by WHO.	Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection, Chapter 2, "HIV diagnosis", Paragraph 2.2 *"National programmes should retest all people newly and previously diagnosed with HIV before they enrol in care and initiate ART."*
Pre-test and post-test advising services.	National guidelines state that pre- and post-test counseling is one of the 5 core components of HIV testing. All those diagnosed with HIV infection should receive counseling after testing and HIV-positive individuals should be referred to the healthcare system (for prevention, treatment, and care).	Consolidated Guidelines on HIV Testing Services, Chapter 3.2.4 Providing pre-test information *"With the widespread use of HIV RDTs, most people receive their HIV test results – at least results of the first test – and often a diagnosis on the same day. Therefore, intensive pre-test counselling is no longer needed and may create barriers to service delivery (51, 52). Individual risk assessment and individualized counselling during the pre-test information session is no longer recommended."*
Testing by non-professional healthcare workers using express diagnostic methods.	Yes, national guidelines provide a regulatory framework for testing in NGOs by non-medical workers. This is described in chapter 4.7 of the Testing of key populations in NGOs: *"...HIV testing in non-governmental organizations should be carried out in full accordance with the testing algorithm using rapid tests. Only trained personnel are allowed to conduct testing..."* *Testing by non-professional medical workers by methods of express diagnostics can be based both on capillary blood and saliva, urine ..."*	Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection, Chapter 2 Paragraph: HIV Testing at the Community Level states that *"in the context of a concentrated HIV epidemic, WHO recommends community-based HIV testing services, with linkage to prevention, treatment and care, in addition to PITC for key populations"*
Testing initiated by a healthcare worker.	Testing initiated by a healthcare worker is included and described in the National Clinical Protocol № 211 "HIV Infection in Adults and Adolescents," Chapter 2.2.2. Screening. Cassette 2 "Epidemiological indications for which healthcare worker should refer patients to be tested for HIV1 / 2 marker." Cassette 3 "List of clinical indications for which HIV 1/2 testing for markers is recommended at the initiative of a healthcare worker based on informed consent."	Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection, Chapter 2 "Diagnosis of HIV Infection", Paragraph 2.4.2 *states that in the context of a concentrated HIV epidemic, provider-initiated testing and counselling (PITC) should be offered for clients (adults, adolescents and children) in clinical settings who present with symptoms or medical conditions that could indicate HIV infection, including presumed and confirmed TB cases.*

Diagnosis of HIV infection in children and infants, in particular, the sensitivity and specificity of tests.	For the diagnosis of HIV infection in children under 18 months of age, the National Guidelines recommend the use of genetic molecular tests (e.g. Xpert Qual). The first test to diagnose possible infection of a newborn, born to HIV + women during pregnancy, is recommended at the age of 48 hours after birth and always before the start of ART for prevention. In case of a negative result in the first 48 hours, a repeated molecular genetic test for HIV DNA is recommended in 2 weeks after the end of preventive treatment. The second test will determine if the infection occurred during child-birth.	Consolidated Guidelines on HIV Testing Services, Chapter "Priority Populations", Item 1 - Infants and Children: *"...It is recommended that all HIV-exposed infants have HIV virological testing at four to six weeks of age or at the earliest opportunity thereafter."*
Testing in special groups - adolescents.	There is no separate chapter in the National Guidelines that describe adolescents testing. The same rules are used for them for testing adults and children over 18 months of age.	Consolidated Guidelines on HIV Testing Services, Chapter 5 "Priority Populations", paragraph 5.2: *"Policies related to the age of consent to testing can pose barriers to adolescents' access to HTS and other health services. The age of consent for HTS varies from country to country. WHO recommends that children and adolescents themselves be involved in the testing decision as much as possible. Governments should revisit age of consent policies in light of adolescents' rights to make choices about their own health and well-being"*
Testing in special groups - pregnant women	According to the National guidelines, pregnant women are tested mandatory once, during pregnancy (upon registration) and they are registered under the code 109.151. The second testing of pregnant women with the first negative test is carried out in the third trimester of pregnancy and only if the woman has an increased risk of infection: serodiscordant family, pregnant women from key groups (PWID, CSW); women who had an increased risk of infection during pregnancy, are indicated under the code 109.152. Rapid testing of pregnant women hospitalized for childbirth in obstetrics is carried out if there is no information about HIV testing during pregnancy using a blood sample and a rapid test.	Consolidated Guidelines on HIV Testing Services, Chapter 5, "Priority Populations", Paragraph 5.3, Pregnant Women, states that *" in low prevalence settings, health-care provider-initiated HIV testing should be considered a recommendation for all pregnant women. In contrast, in low prevalence* *settings, retesting all pregnant women in ANC or in the breastfeeding period is* *not warranted, as the incidence of HIV infection will be extremely low."*
Testing in special groups - couples and partners	According to the National guidelines, HIV testing services for couples and partners can be conducted in different locations using the same algorithm.	Consolidated Guidelines on HIV Testing Services, Chapter 5 "Priority Populations", Paragraph 5.4 *"Couples and Partners" recommends "In low-level and concentrated epidemics, couples and partner HTS should be made available for partners of people with HIV and people from key populations".*

Diagnostic algorithms	In the National guidelines, the algorithm for diagnosing HIV infection is based on the WHO recommendation: 2 blood samples - 3 tests for making a diagnosis of HIV in low-prevalence settings. But the main difference is the use of an HIV RNA test as a 3rd study (molecular genetic test). *"... Screening for HIV infection is carried out by means of express diagnostics, preferably III and IV generations.* ***On the first-line assay (A1 - baseline test),*** *you must use the rapid test with the highest possible sensitivity. If the result is reactive (positive), another blood sample should be collected and tested with an alternative rapid diagnostic test.* ***On the second-line assay (A2 - alternative test),*** *it is necessary to use a test with specificity not less than that used for screening testing on the first-line assay (A1). As in the case of the first-line assay (A1), testing used in the second-line assay (A2) must use diagnostic rapid tests, at least III generation, and always from a different manufacturer than the one whose tests were used in A1. Testing on the second-line assay (A2) should be carried out in the laboratories of the ART centers.* *In case of a reactive (positive) result, this sample must be confirmed using the III line of testing (molecular genetic test).* ***The third-line assay (A3 - confirmatory test)*** *must use a molecular genetic test based on the quantitative detection (RNA) of HIV 1, therefore, for samples reactive in the first and second assays (A1 +, A2 +), it is necessary to use a separate and defined third assay (A3) for a positive diagnosis of HIV 1."*	7.2.2 Serological testing strategy for HIV diagnosis in low prevalence settings: *All specimens are first tested with one assay (A1), and specimens that are non-reactive (A1−) are considered HIV-negative and reported as such. A1 should be the most sensitive assay available, taking into account diagnostic sensitivity, seroconversion sensitivity and analytical sensitivity.* *Any specimens that are reactive on the first-line assay (A1+) should be retested using a separate and distinct second assay (A2) comprising a different antigen preparation to avoid false cross-reactivity with A1.* *In a low prevalence population, the positive predictive value based on two test results is too low to provide an HIV diagnosis. Therefore, for specimens that are reactive on the first and the second assays (A1+; A2+), a third separate and distinct assay (A3) should be used to confirm the results and issue an HIV-positive diagnosis".*

Part 3. ARV drugs for HIV prevention

Information on ARV drugs for HIV prevention is indicated in 3 main regulatory documents:

1. **National Clinical Protocol No. 316 "Prevention of mother-to-child transmission of HIV" approved by the order of the MHLSP, No. 166, dated February 07, 2018.**
2. **National Clinical Protocol No. 314 "Post-exposure prophylaxis of HIV infection" approved by the order of the MHLSP, No. 164, dated February 07, 2018.**
3. **National Clinical Protocol No. 313 "Pre-exposure prophylaxis of HIV infection" approved by the order of the MHLSP, No. 162, dated February 07, 2018.**

	Recommendations of national protocols and guidelines	WHO recommendations
Pre-exposure prophylaxis of HIV infection	According to NCP № 313, PrEP is intended for people at high risk of HIV infection. PrEP should be made available to all individuals wishing to use PrEP if they meet the eligibility criteria for PrEP. The NCP recommends continuous use of PrEP with TDF + FTC. NCP № 313 clearly states the indications and contraindications for PrEP, the plan for managing the patient on PrEP (the frequency of consultations, and the required examination plan).	The Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection states that oral *"Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches..."*
Algorithm and regimens of post-exposure prophylaxis for different population groups	According to NCP № 314, Post-Exposure Prophylaxis of HIV Infection, *PEP should be offered to anyone at risk of HIV infection within 72 hours, according to Cassette 9: "TDF + 3TC will be the backbone regimen. LPV/r will be recommended as the third drug. If possible, the use of RAL, DRV/r or EFV can be analyzed as an alternative regimen. The duration of treatment is 28 days."*	The Consolidated Guidelines for the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection states that *"HIV PEP should be offered and initiated as early as possible in all individuals with an exposure that has the potential for HIV transmission, preferably within 72 hours..."* ARV regimens for HIV post-exposure prophylaxis for adults and adolescents: · TDF + 3TC (or FTC) is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis in adults and adolescents. · LPV/r or ATV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for adults and adolescents.

Algorithm and regimens of post-exposure prophylaxis for PMTCT.	The algorithm and schemes of PEP for PMTCT are described in the National Clinical Protocol № 316 "Prevention of mother-to-child transmission of HIV". The main drug for PEP for newborns, born to HIV-infected mothers, is ZDV syrup at a dose of 4 mg/kg 2 times a day for 28 days. If the mother had detectable HIV RNA at the time of delivery, such a newborn is recommended, in addition to the ZDV syrup, 3 doses of NVP syrup 12 mg at 1, 3, and 7 days of life.	The WHO guidelines on the prevention of infant prophylaxis if the maternal is on ART have not changed since 2010. It is recommended that breastfed infants receive NVP daily for 6 weeks, and non-breastfed infants receive either AZT once daily or NVP twice daily for 4-6 weeks. Breastfed infants who are at high risk of HIV infection, and infants newly exposed to HIV during the postpartum period, should continue prophylaxis for another 6 weeks (12 weeks total, infant prophylaxis) using either AZT (twice a day) and NVP (once a day), or NVP only.

Part 4. Antiretroviral therapy regimens

Antiretroviral therapy regimens are described in the following regulatory documents:

1. **National Clinical Protocol No. 211 "HIV infection in adults and adolescents" approved by the order of the MHLSP, No. 163, dated February 07, 2018.**
2. **National Clinical Protocol No. 315 "HIV infection in children 0-10 years old" approved by the order of the MHLSP, No. 165, dated February 07, 2018.**

	Recommendations of national protocols and guidelines	WHO recommendations
When ART should be started, including recommendations for specific groups of patients (for whom urgent indication is recommended).	According to the NCP No. 211 and NCP No. 315 Indications for starting ART are as follows: *"Treatment is recommended for all patients, regardless of the stage of the disease and for any CD4 count."* In contrast to the WHO Guidelines, the NCP does not prioritize the prescription of ART for patients with more severe and advanced stages of HIV infection. This was done intentionally to exclude the possibility of refusal to ART in cases of normal health and lack of immunodeficiency at the time of the visit to the doctor to receive ART.	According to the Consolidated Guidelines for the Use of ARVs for Treating and Preventing HIV Infection, Chapter 4.3: *ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count. As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤350 cells/mm3."* *ART should be initiated in all children living with HIV, regardless of WHO clinical stage or at any CD4 cell count; Infants diagnosed in the first year of life; Children living with HIV 1 year old to less than 10 years old.* *As a priority, ART should be initiated in all children <2 years of age or children younger than 5 years of age with WHO clinical stage 3 or 4 or CD4 count ≤750 cells/mm³ or CD4 percentage <25% and children 5 years of age and older with WHO clinical stage 3 or 4 or CD4 count ≤350 cells/mm³"*

Choosing first-line drugs, including:

- Preferences for fixed-dose combination (FDCs) drugs.
- Refusal to use stavudine.
- Use of DTG and EFV400 following the updated recommendations (2018, 2019).
- Recommendations for use of dolutegravir in women of childbearing age and pregnant women.

First-line ART recommended by the NCPs No. 211 and No. 315:

First-line ART	Preferred regimen	Alternative regimen
Adult patients	TDF + 3TC (or FTC) + DTG	TDF + 3TC (or FTC) + EFV
Women of childbearing age	TDF + 3TC (or FTC) + EFV	TDF + 3TC (or FTC) + ATV/r (or LPV/r)
Patients receiving rifampicin-based TB treatment	TDF + 3TC (or FTC) + EFV	TDF + 3TC (or FTC) + DTG double dose
Children 0 to 6 years old	ABC + 3TC + LPV/r	AZT + 3TC + RAL
Children and adolescents older than 6 years old	ABC + 3TC +DTG	AZT + 3TC + LPV/r (or RAL)

According to the WHO Guidelines, the NCP also recommends giving preference to the combination ART regimen of the 3 drugs combination in one tablet once a day.

Since 2010, Stavudine has not been used in Moldova.

DTG is not recommended for women of childbearing age.

DTG-based combination drugs are recommended as the main first-line treatment regimen for adults and adolescents. An EFV 600 mg regimen is recommended for women of childbearing age and patients receiving Rifampicin-based TB treatment.

First-line ART recommended by the Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection, 2016

First-line ART	Preferred regimen	Alternative regimen
For adult patients	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + DTG TDF + 3TC (or FTC) + EFV400 TDF + 3TC (or FTC) + NVP
Women who are pregnant or breastfeeding	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + NVP
Adolescents	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV (or NVP) TDF (or ABC) + 3TC (or FTC) + DTG TDF (or ABC) + 3TC (or FTC) + EFV400 TDF (or ABC) + 3TC (or FTC) + NVP
Children 3 to 10 years of age	ABC + 3TC + EFV	ABC + 3TC + NVP AZT + 3TC + EFV (or NVP) TDF + 3TC (or FTC) + EFV (or NVP)
Children younger than 3 years of age	ABC (or AZT) + 3TC + LPV/r	ABC (or AZT) + 3TC + NVP

Recommendations for breastfeeding of babies

The NCP No. 316 “Prevention of mother-to-child transmission of HIV “, as one of the PMTCT components, recommends artificial feeding of a newborn born from an HIV-infected woman is. All these children are provided with formula feeding free of charge. Pregnant women should be advised that if they are tested in advance, they will have 100% adherence to ART and their VL will be undetectable, they can choose to breastfeed their newborn. Cassette 9, “Feeding a Newborn, Born to an HIV-Infected Mother”, contains recommendations for both formula feeding and breastfeeding. Despite the strong recommendations of the NCP, the woman has the right to choose the way of feeding.

The 2012 WHO guidelines focus on encouraging and supporting breastfeeding of infants by HIV-infected mothers up to 12 months of age. This guideline recognizes that some mothers cannot provide safe and sufficient nutrition to children under 12 months of age without breastfeeding. In these situations, it is suggested to continue breastfeeding while the mother is on ART. WHO is currently reviewing the feasibility of recommending unrestricted breastfeeding for HIV-infected women on ART.

Monitoring before and after starting ART	According to the NCP No. 211 and 315: • **Hemoleukogram, biochemical blood test, screening for syphilis, HbsAg and total antibodies to HCV, gynecological examination with a Pap smear** are at the patient's first visit, then once a year, then if necessary; • **Cryptococcal antigen -** when the number of CD4 lymphocytes is less than 100 cells/mm3 and there are clinical signs of cryptococcosis (fever); • **HLA-B*5701 -** when planning the appointment of ABC; • **Antibodies of IgG class to toxoplasma** with CD4 <200 cells/mm3 ; • **Ophthalmic examination** if CD4 count is below 100 cells/mm3. • **Clinical screening for TB.** At every visit of PLHIV to an infectious disease specialist, TB screening should begin with at least one of the following 4 symptoms: · cough, · temperature, · weight loss, · night sweats. If PLHIV complains of at least one of the clinical symptoms typical of pulmonary TB or extrapulmonary TB, or recent contact with a TB patient has been identified, a complete screening for active TB is required. To confirm or exclude TB, it is necessary to conduct: · Clinical examination; · Xpert MTB/RIF; · X-ray examination; · Microscopy of sputum for BAAR; · Bacteriological examination of sputum (rapid methods); · Referral to a TB specialist. • **CD4 level:** · t the time of HIV detection and/or ART initiation; · every 6 months, if the CD4 count is 350 cells/mm3 before the patient becomes adherent to the treatment and if the CD4 count is> 350 cells/mm3 - once a year; · if a virological failure is suspected. • **PCR viral load test:** · at the time of HIV detection and/or ART initiation; · every 6 months in case of viral suppression; · when changing the ART regimen after 8-12 weeks; · if a virological failure is suspected.	Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection, Table 4.10. Recommended tests for HIV screening and monitoring and approaches to screening for coinfections and noncontagious diseases. **ART initiation :** · Hemoglobin test for starting AZT · Pregnancy test · Blood pressure measurement · Serum creatinine and estimated glomerular filtration rate (eGFR) or starting TDF · Alanine aminotransferase for NVP · Baseline CD4 cell count. **Receiving ART:** · HIV viral load (at 6 months and 12 months after initiating ART and every 12 months thereafter) · CD4 cell count every 6 months until patients are stable on ART · In settings where routine viral load monitoring is available, CD4 cell count monitoring can be stopped in individuals who are stable on ART and virally suppressed.

<table>
<tr>
<td>Recommendations for switching to second-line ART regimens, including special patient populations</td>
<td>Second-line ART is the next treatment regimen used immediately after first-line ART has failed. Ritonavir-boosted PIs are commonly used in the second-line regimen.
<table>
<tr><th>1st-line</th><th>2nd- line</th></tr>
<tr><td>TDF + FTC /3TC + DTG (EFV)</td><td>AZT + 3TC/FTC + ATV/r or LPV/r or DRV/r</td></tr>
<tr><td>ABC + 3TC+ DTG (EFV)</td><td>TDF + FTC/3TC + ATV/r or LPV/r or DRV/r</td></tr>
</table>
after LPV/r as the main second-line drug in children under 6 years of age. In children over 6 years of age, following a failure on DTG regimens, LPV/r is recommended with two other NRTIs.</td>
<td>Second-line ART by the Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection, 2016
<table>
<tr><th></th><th>1st-line</th><th>2nd-line</th><th>2nd-line alternative</th></tr>
<tr><td>Adults and adolescents</td><td>Two NRTI +EFV (DTG)</td><td>Two NRTI + ATV/r or LPV/r</td><td>Two NRTI + DRV/r</td></tr>
<tr><td rowspan="2">Children younger than 3 years of age</td><td>2 NRTI+ LPV/r</td><td>2 NRTI + RAL</td><td>Continue and switch to 2 NRTIs + EFV over 3 years of age</td></tr>
<tr><td>2 NRTI + NVP</td><td>2 NRTI + LPV/r</td><td>2 NRTI +RAL</td></tr>
<tr><td rowspan="2">Children aged 3 to 10 years of age</td><td>2 NRTI + LPV/r</td><td>2 NRTI + EFV</td><td>2 NRTI +RAL</td></tr>
<tr><td>2 NRTI + EFV</td><td>2 NRTI +LPV/r</td><td>2 NRTI + ATV/r</td></tr>
</table></td>
</tr>
<tr>
<td>Recommendations for the third-line ARVs</td>
<td>The recommendations for the third line in the NCP for the treatment of adults and adolescents do not differ from those recommended by WHO: it is also recommended regimens based on DRV/r 600/100 mg 2 times a day, in combination with 2 NRTIs + or NNRTI (or DTG), depending on to what the sensitivity is.</td>
<td>According to the Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection:
· National programs should develop policies for third-line ART
· Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as INSTIs and second-generation NNRTIs and PIs.</td>
</tr>
<tr>
<td>Barriers to accessing key drugs recommended by WHO, when they are available (e.g., no registration, no inclusion in the list of vital and essential medicines or procurement lists, high price, etc.)</td>
<td>The purchase of ARV drugs that are not registered in RM is allowed, but the preference is still given to registered drugs, which can be much more expensive than unregistered ones. In this regard, during public procurement in 2014, one of the drugs was purchased at a price that was almost 10 times higher than the purchase price from the Global Fund.
The availability of a small number of children under 10 years on ART in RM (about 70 people) makes it difficult to purchase children's forms.</td>
<td>N/A</td>
</tr>
<tr><td colspan="3">Part 5. Prevention and treatment of concomitant infections and diseases</td></tr>
<tr>
<td></td>
<td>Recommendations of national protocols and guidelines</td>
<td>WHO recommendations</td>
</tr>
<tr>
<td>Recommendations for the prevention and treatment of co-infections, primarily (but not limited to):
· HIV/HCV
· HIV/HBV
· HIV TB</td>
<td>Recommendations for the treatment of co-infections (HIV/HCV, HIV/HBV, HIV/TB) are specified in the corresponding protocols for the treatment of HCV, HBV, TB.
The NCP № 211 and NCP № 315 have separate annexes that describe the prevention of opportunistic infections. Both protocols recommend TB prevention and describe regimens and doses for TB prevention.</td>
<td>According to the Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection, 2016: “Adults and adolescents living with HIV who have an unknown or positive tuberculin skin test (TST) status and are unlikely to have active TB should receive at least 6 months of IPT as part of a comprehensive package of HIV care. IPT should be given to such individuals regardless of the degree of immunosuppression and also to those on ART, those who have previously been treated for TB and pregnant women.</td>
</tr>
</table>

Prevention and treatment of relevant non-communicable diseases: • Cardiovascular diseases • Depression • Diseases of the central nervous system • Kidney diseases • Substance use	The NCP does not describe the prevention and treatment of non-communicable diseases.	According to the Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection, 2016: 1. Assessment and management of cardiovascular risk should be provided for all individuals living with HIV according to standard protocols recommended for the general population 2. Assessment and management of depression should be included in the package of HIV care services for all individuals living with HIV 3. WHO experts recommend using a comprehensive package of prevention, treatment and care measures for HIV-infected PWID.
Part 6. Health service provision		
The provision of health services, including but not limited to: • Recommendations for the decentralization of services. • Recommendations for redistribution and delegation of services. • Recommendations for integration of services.	The NCP describes the activities for the prevention, diagnosis, and treatment of HIV infection for different levels of care (primary, specialized, and inpatient). Issues on decentralization and integration of services are beyond the scope of the NCP and can be described in the National Program and other regulative documents.	
Part 7. Other clinically significant discrepancies that do not fall under the thematic blocks indicated above		
Other, known to the expert, clinically significant discrepancies between the WHO Guidelines on the diagnosis and use of antiretroviral drugs and national recommendations, for example, on the provision of harm reduction services for patients who use psychoactive substances, etc.	No other clinically significant discrepancies were found.	

Consolidated recommendations for optimizing HIV treatment protocols in Moldova:

Based on the analysis, it should be noted that in the Republic of Moldova the regulatory framework in the field of HIV is more in line with the 2016 WHO Guidelines but, due to new recommendations, the following changes can be advised:

The National guidelines for laboratory diagnostics of HIV infection are almost completely correspond to the WHO Guidelines but the main difference is the use of molecular genetic testing as the third confirmatory diagnostic method.

In case of revision of these guidelines, it is possible to recommend:

1. Considering adding another 3rd test for antibodies to HIV (serological) at the age of 9 months to exclude a possibly false-negative result for HIV when diagnosing HIV infection in exposed infants with HIV up to 18 months.

2. The National Guidelines should include information on testing adolescents, which will include age limits regarding consent to testing, as well as specifics of counseling adolescents before and after testing.

3. In the chapter on testing pregnant women, recommending HIV testing also to sexual partners of pregnant women to prevent possible HIV infection during pregnancy and breastfeeding using a specific testing code, which will monitor the level of implementation of this recommendation.

National Clinical Protocol No. 211 "HIV infection in adults and adolescents" also largely complies with the WHO Guidelines but due to new recommendations that have appeared in July 2019, it is recommended to revise it with the inclusion of the following proposals:

1. Specify the peculiarities of initiating ART in patients with severe opportunistic infections, including TB.

2. The first-line ART regimens prescribed in the NCP differ slightly from the 2016 WHO Guidelines but practically, to a greater extent, they correspond to the WHO Guidelines of July 2019 and, therefore, do not require changes.

3. Recommendations for second-line ART in adults and adolescents in the NPC should be changed in accordance with the WHO Guidelines of July and, as the preferred second-line drug, in case of failure on NNRTI, dolutegravir should be used, and in case of failure on dolutegravir, boosted IP ATVs or LPV/r in combination with two other NRTIs should be recommended.

4. For more optimal use of financial resources, it is necessary to revise monitoring after the initiation of ART, namely the frequency of tests to determine CD4 counts and viral load on continuous ART to decrease the number of VL testing for the first time after 6 months of ART and then 1 time in 12 months, and on CD4 once every 6 months, if CD4 account is less than 350 cells, to determine the need for prophylaxis of opportunistic infections and it is possible to stop monitoring the number of CD4 cells while stable on ART: CD4 count is more than 350 cells and undetectable viral load.

5. It is necessary to include in the HIV NCP links to documents that provide recommendations for the prevention and treatment of co-infections (HBV, HCV, TB) so that physicians can quickly find these peculiarities or briefly describe them in an appropriate protocol.

6. It is very important in this protocol to describe the assessment and control of the risks of some non-communicable diseases: the assessment of the risk of CVD, kidney diseases, and the development of depression. It is necessary to develop questionnaires for each of these diseases or adapt existing ones, and to assess the risk at each visit and, if early signs are detected, to refer the patient to the appropriate specialists.

National Clinical Protocol No. 315 "HIV infection in children 0-10 years old"

1. Recommendations for first-line ART in children younger than 10 years in the NCP should be adapted to the latest 2019 WHO Guidelines and include recommendations to use RAL as the main drug for the treatment of newborns.

2. Recommend adding to the algorithm of HIV testing in exposed infants with HIV

National Clinical Protocol No. 316 "Prevention of mother-to-child transmission of HIV"

1. Recommend also HIV testing to sexual partners of pregnant women to prevent possible HIV infection during pregnancy and breastfeeding.

2. Regarding feeding infants born to HIV-infected mothers, encourage and support breastfeeding more but only with adherence to ART.

National Clinical Protocol No. 314 "Post-exposure prophylaxis of HIV infection"

1. In accordance with the latest 2019 WHO Guidelines, it is necessary to substitute DTG for LPV/r in the recommendation of the NCP on the preferred third drug for post-exposure prophylaxis of HIV in adults and adolescents, as well as children of appropriate age.

2. Due to the fact that, when switching to the use of DTG-based treatment regimens as PEP, the cost of medicines for PEP is significantly reduced, it is recommended to maximize access to these medicines, providing both the medicines themselves and short information on prescribing and taking PEP.

National Clinical Protocol No. 313 "Pre-exposure prophylaxis of HIV infection"

1. In accordance with the latest 2019 WHO Guidelines, the NCP should be included by:

   - Use of short courses of PrEP (2 + 1 + 1) by men who have sex with men;
   - Use of the TDF + 3TC drug, which has also been approved by the WHO for PrEP;
   - Change the period of taking ARV drugs if PrEP is discontinued from 28 days to 7 days.

At the same time, it is necessary to prescribe the algorithm for choosing between short PrEP courses and those on an ongoing basis.

2. Due to the demand for the community-based PrEP as a result of the NCP № 162 implementation, it is necessary to specify peculiarities of community-based PrEP.

Russia

Part 1. Basic information	
Name of the current version of the document and the link to it	Clinical guidelines "HIV infection in adults"
Year of the current version.	2017
The normative document number and its status (order, resolution, if applicable).	CG79
Legal status of recommendations: mandatory or advisory (What additional documents govern the need for recommendations).	It is recommendatory, but the following is legally fixed. According to the Federal Law of December 25, 2018, № 489-FZ "On Amendments to Article 40 of the Federal Law 'On Compulsory Health Insurance in the Russian Federation' and the Federal Law 'On the Basics of Health Protection of Citizens in the Russian Federation' on clinical guidelines": "Health care, except health care provided in the framework of clinical approbation, is organized and provided based on... clinical guidelines." *Article 37: "7. For each disease ... for adults and children, no more than one clinical guideline can be agreed and approved respectively. 8. In the event that the scientific-practical council receives several clinical guidelines for one disease... from several medical professional non-profit organizations, the scientific-practical council either decides to approve one of the received clinical guidelines or organizes work on joint development.... organizations that sent these clinical guidelines, one clinical guideline".*
Frequency of the document revision (Is it defined? What documents regulate this?).	Determined - two years. The form complies with the Order of the Ministry of Health of Russia dated February 28, 2019, № 103n "On the approval of the procedure and terms for the development of clinical guidelines, their revision, the standard form of clinical guidelines and requirements for their structure, composition and scientific validity of information included in the clinical guidelines"
Level of evidence (description of the applicable system).	Methods used to assess the quality and strength of evidence: · Reviews of published meta-analyses; · Systematic reviews with tables of evidence; · Expert consensus; · Assessment of significance in accordance with the rating scheme. The evidence base for the recommendations was the publications included in the Cochrane Library, EMBASE, PUBMED, and MEDLINE databases. Selection of publications as potential sources of evidence is conducted according to the level of validity of each study. Impact of the evidence assigned to a publication on the strength of the recommendations arising from it. To minimize potential bias due to subjective factors, each study was evaluated independently by at least two independent members of the working group. Differences in ratings were discussed by the whole group. In the absence of consensus, independent experts were recruited from among the most experienced specialists of the local AIDS centers. **Grades of Evidence Level:** **High.** The likelihood that further research will change our confidence in the estimate of the effect is very low. **Middle.** Further research may significantly affect our confidence in the estimate of the effect and may change the estimate. **Low.** The likelihood that further research could influence the effect estimate and change it very high. **Very low.** Any estimate of the effect is highly uncertain.
Members of the editorial board (Are representatives of NGOs/patient organizations included?).	The recommendations were compiled by the authors of the National Association of Specialists in the Prevention, Diagnosis, and Treatment of HIV Infection. Working group: Voronin E.E., Afonina L.Y., Rosenberg V.Y., Latysheva I.B., Kaminsky G.D., Bulankov Y.I., Melnikova T.N., Radzikhovskaya M.V, and Fomin Y.A. The working group did not include representatives of patient organizations.

List and a brief description of documents that additionally regulate the use of ARVs in the country, including the following documents, but not limited to: • Laws governing the nature of supplying the ARVs (free of charge/paid, by prepaid medical care plan or at the expense of a special national program, etc.); • Lists of vital and essential medicines; • Lists of medicines to be procured at the expense of different budgets; • Treatment standards, etc.	**Treatment**: Order of the Ministry of Health of Russia dated November 20, 2018, No. 796n "On approval of the standard of primary health care for adults with an illness caused by the human immunodeficiency virus (HIV) (examination to establish a diagnosis and prepare for treatment)". Order of the Ministry of Health of Russia dated November 20, 2018, No. 797n "On approval of the standard of primary health care for adults with an illness caused by the human immunodeficiency virus (HIV) (preferred first-line antiretroviral therapy)." Order of the Ministry of Health of Russia dated November 20, 2018, No. 798n "On approval of the standard of primary health care for adults with an illness caused by the human immunodeficiency virus (HIV) (alternative first-line antiretroviral therapy)." Order of the Ministry of Health of Russia dated November 20, 2018, No. 799n "On approval of the standard of primary health care for adults with an illness caused by the human immunodeficiency virus (HIV) (special cases of first-line antiretroviral therapy)." Order of the Ministry of Health of Russia, dated November 20, 2018, No. 800n "On approval of the standard of primary health care for adults with an illness caused by the human immunodeficiency virus (HIV) (preferred second-line antiretroviral therapy)." Order of the Ministry of Health of Russia dated November 20, 2018, No. 801n "On approval of the standard of primary health care for adults with an illness caused by the human immunodeficiency virus (HIV) (alternative second-line antiretroviral therapy)." Order of the Ministry of Health of Russia dated November 20, 2018, No. 802n "On approval of the standard of primary health care for adults with an illness caused by the human immunodeficiency virus (HIV) (third-line antiretroviral therapy)." Terminated - the order of the Ministry of Health of the Russian Federation, dated December 24, 2012, No. 1511n "On approval of the standard of primary health care in case of illness caused by the human immunodeficiency virus (HIV)." Order of the Ministry of Health of the Russian Federation, dated November 8, 2012, No. 689n "On approval of the procedure for providing medical care to the adult population with an illness caused by the human immunodeficiency virus (HIV)." Besides, to treat patients, the physician should use the instructions for the medicines. According to the order of the Ministry of Health of the Russian Federation No. 88, dated March 26, 2001, the instruction is an official document containing sufficient information. The drug must be included in the State Register of Medicines http://grls.rosminzdrav.ru/GRLS.aspx. According to the Order of the Ministry of Health and Social Development No. 494, dated August 09, 2005, "On the procedure for the use of drugs in patients for health reasons," to appoint the drug that does not have a registration, a decision of a medical council of a specialized Federal institution, a protocol and a signature of the chief physician are required. For children - separate recommendations, including PMTCT: Clinical guidelines "HIV infection in children" CR 459 2017, approved by the Ministry of Health of the Russian Federation. **Regulation of purchases:** Resolution of the Government of the Russian Federation dated December 19, 2016, №1403 "On the Program of State Guarantees of Free Medical Assistance to Citizens for 2017 and the Planning Period of 2018 and 2019" - purchase of antiviral drugs included in vital and essential medicines list for treatment of people infected with HIV at the expense of budgetary allocations from the federal budget, including in combination with hepatitis B and C viruses. Resolution of the Government of the Russian Federation dated December 28, 2016, No. 1512 "On approval of the Regulation on the organization of provision of persons infected with the human immunodeficiency virus, including in combination with hepatitis B and C viruses, antiviral drugs for medical use, the Regulation on the provision of persons with tuberculosis with multidrug resistance of the pathogen, antibacterial and anti-tuberculosis drugs for medical use"- purchases made by the Ministry of Health of RF. Only ARVs included in the vital and essential medicines list. Resolution of the Government of the Russian Federation, dated November 15, 2017, No. 1380 "On peculiarities of the description of medicinal products for medical use, which are the object of procurement to meet state and municipal needs" does not allow specifying the need for a fixed-dose combination, exact dosage, temperature storage regime. Suppliers may offer mono-preparation, less convenient dosages. Order of the Government of the Russian Federation, dated December 10, 2018, № 2738-r "On approval of the list of vital and essential medicines for medical use for 2019..." includes 24 INNs for the treatment of HIV infection, Resolution of the Chief State Sanitary Doctor of the Russian Federation, dated February 13, 2012, No. 16 "On urgent measures to counter the spread of HIV infection in the Russian Federation."

	State guarantees: Federal Law of March 30, 1995, No. 38-FZ "On the prevention of the spread in the RF of a disease caused by the human immunodeficiency virus (HIV)." (Article 4) - the state guarantees the availability of medical examination to detect HIV infection and free provision of medicines for medical use to treat HIV infection. Federal Law, dated March 30, 1999, No. 52-FZ "On the Sanitary and Epidemiological Welfare of the Population." Federal Law, dated November 21, 2011, No. 323-FZ "On the Fundamentals of Health Protection of Citizens in the Russian Federation" (Collection of Legislative acts of the Russian Federation, 2011, No. 48, Art. 6724). - Prescription and use of medicinal products for medical use ... that are not included in the standard of medical care allowed in the presence of medical indications (individual intolerance, for health reasons) by the decision of the medical commission (part 5, Article 37).
Other significant information	Infectious disease specialists of the Russian Federation traditionally used the Clinical Recommendations of the Federal AIDS Center. However, the new law excludes the use of alternative recommendations. It is extremely important to update the standards that have been in effect in the country since 2012.

Page and quote from national protocols	Comment	Link to relevant WHO recommendation
Part 2. Diagnostic recommendations		
Retesting before inclusion in care and treatment programs: Page 21 "Confirmatory tests (immune, linear blot) are recommended to confirm HIV results."	Really available. It is not specified about the second specimen. However, this is approved by other regulatory documents. It is of great importance that IB is now performed from the first blood specimen.	**The 2016 WHO Guidelines, page 27** Retest all clients diagnosed HIV-positive with a second specimen and a second operator using the same testing strategy and algorithm before enrolling the client in care and/or initiating ART, regardless of whether or not ART initiation depends on CD4 count.
Page 21. It is recommended to use the determination of HIV RNA or DNA by molecular biological methods to confirm the diagnosis in persons who are in the period of the "serological window"..., as well as when receiving a negative and doubtful result of an immune or linear blot after a positive result in a screening test. If a negative and doubtful result is obtained in an immune or linear blot, it is recommended to examine a biological sample in a test system to determine the p25/24 antigen or HIV DNA/RNA.	This makes it possible to examine patients in the "serological window". It is most likely not available in all territorial AIDS centers.	
Comments: HIV gene material can be detected already at the 7th day after infection, p24 antigen - at the 15th, the first antibodies - on the 30th, late - by 3 months.	This is a very valuable commentary showing the current state of the HIV diagnostics. Previously, it was recommended the examination for up to 12 months.	
It is recommended to use indicators of the absolute CD4 count in adults to determine the first, second and third immune categories (no immunodeficiency, moderate, marked or severe immunodeficiency), to determine severe immunodeficiency are indicators of the absolute CD4 count and CD4 percentage.		
Pre-test and post-test advising services	It does not comply	
Testing by non-professional healthcare workers using express diagnostic methods.	It does not comply	Lay providers who are trained and supervised can independently conduct safe and effective HIV testing using rapid diagnostic tests (strong recommendation, moderate-quality evidence).
Testing initiated by a healthcare worker.	It is not specified	

Diagnosis of HIV infection in children and infants, in particular, the sensitivity and specificity of tests. Not reflected. However, this is described in the 2017 Clinical Guidelines for HIV Infection in Children. It is recommended to examine children born to mothers whose blood antibodies to HIV are detected before pregnancy, during pregnancy, during childbirth or breastfeeding. Strength of recommendations - A (level of evidence - 1a). HIV diagnostics by PCR is recommended - methods are used to detect HIV NA in the child's blood (DNA or HIV RNA). If there is a high risk of infection, it is recommended to carry out diagnostics in the first 48 hours of life in the maternity hospital (blood from the umbilical cord cannot be examined). Strength of recommendation - B (level of evidence - 2a) Comments: a high risk of infection is considered to be the absence of any of the PMTCT stages, the determined level of HIV VL in the mother by 36 weeks of pregnancy, the presence of clinical manifestations of intrauterine infection - prescribe ART as soon as possible. It is recommended that the first mandatory testing for HIV NA be performed at the age of 4-6 weeks.	It does not generally comply. The sensitivity and specificity of test systems are not specified. The dry drop method is not implemented.	**The 2016 WHO Guidelines, page 28** It is strongly recommended that HIV serological assays used for the purpose of clinical diagnostic testing have a minimum sensitivity of 99% and specificity of 98% under quality-assured laboratory conditions (strong recommendation, moderate-quality evidence). It is strongly recommended that HIV virological assays used for the purpose of clinical diagnostic testing (usually at or after 6 weeks of age) have a sensitivity of at least 95% and ideally greater than 98%, and specificity of 98% or more under quality-assured, standardized and validated laboratory conditions (strong recommendation, moderate-quality evidence). It is strongly recommended that HIV virological testing be used to diagnose HIV infection in infants and children below 18 months of age (strong recommendation, high-quality evidence). In infants and children undergoing virological testing, the following assays (and respective specimen types) are strongly recommended for use: HIV DNA on whole blood specimen or DBS; HIV RNA on plasma or DBS; Us p24 Ag on plasma or DBS (strong recommendation, high-quality evidence). It is strongly recommended that all HIV-exposed infants have HIV virological testing at 4–6 weeks of age or at the earliest opportunity thereafter (strong recommendation, high-quality evidence).
Testing in special groups (adolescents, pregnant women, couples, and partners).	Not reflected.	
Part 3. ARV drugs for HIV prevention		
Pre-exposure prophylaxis of HIV infection Not specified.	There is no regulatory framework at all in the Russian Federation.	
Algorithm and regimens of post-exposure prophylaxis for different population groups, including PMTCT Not specified.	Recommendations for PEP for medical workers are reflected in SP 3.1.5.2826-10.	
Part 4. Antiretroviral therapy regimens		
When ART should be started, including recommendations for specific groups of patients (for whom urgent indication is recommended).		
Page 25. Indications for initiating ART ART is recommended for all HIV patients. A strong recommendation (medium confidence). *The period between the identification of indications for ART and its initiation should be as short as possible.*	It complies.	**The 2016 WHO Guidelines, page 33 When to start ART** ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count (strong recommendation, moderate-quality evidence).

Pages 25-26. It is recommended to start ART as an emergency (no later than 1 week) in the following cases: · with a CD4 count of fewer than 200 cells/mm3. A strong recommendation (high confidence). **Page 26. It is recommended to start ART on a priority basis (no later than 2 weeks) if:** · clinical stages 2B, 2B, 4 and 5 according to the Russian classification; · with a CD4 count of fewer than 350 cells/mm3; · VL> 100,000 copies/ml; · chronic viral hepatitis B requiring treatment; · diseases requiring long-term use of therapy that suppresses immunity; · the need to use ART.	It generally complies. I believe that the more additional criteria for early initiation of ART, the more reasons to postpone therapy.	**The 2016 WHO Guidelines, page 33** As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with a CD4 count ≤350 cells/mm3 (strong recommendation, moderate-quality evidence).
Pages 25-26. It is recommended to start ART as an emergency (no later than 1 week) in the following cases: · upon detection of HIV infection in a pregnant woman at a gestational age of 13 weeks or more. A strong recommendation (high confidence level); · when HIV infection is detected in a pregnant woman with CD4 less than 350 cells/ mm3 and/or VL> 100,000 copies/ml at a gestational age of fewer than 13 weeks. A strong recommendation (high confidence level) *Comments: During the admission under the supervision of an HIV-infected pregnant woman at 28 weeks gestation or more, antiretroviral therapy should be started at least 3 days regardless of indications and VL.*	It does not comply, because the possibility of postponing therapy is allowed.	ART should be initiated in all pregnant and breastfeeding women living with HIV, regardless of WHO clinical stage and at any CD4 cell count and continued lifelong (strong recommendation, moderate-quality evidence).
Choice of first-line drugs, incl.		
Page 25 The preferred regimen for adults: TDF + 3TC (or FTC) + EFV (Approved by the Order of the MoH of RF, № 797). Alternative regimen for adults: TDF + 3TC + NVP (or DTG); ABC + 3TC + NVP (or DTG); ABC + 3TC + DTG (or EFV); AZT (F-AZT) + 3TC + EFV (or NVP or DTG) (Approved by Order of the MoH of RF, № 798).	Does not match. The preferred mode does not contain DTG. EFV 400 is missing.	**The 2019 WHO Guidelines, page 7** Preferred regimen for adults: TDF + 3TC (or FTC) + DTG. Alternative regimen for adults: TDF + 3TC + EFV 400 mg. Preferred regimen for children: ABC + 3TC + DTG. Alternative regimen for children: ABC + 3TC + LPV r or ABC + 3TC + RAL or TAF + 3TC (or FTC) + DTG. Preferred regimen for neonates: AZT + 3TC + RAL. Alternative regimen for neonates: AZT + 3TC + NVP.
Fixed-dose combination (FDC) preferences **Page 24.** It is recommended if the first-line ART (starting ART) is prescribed using the less toxic and more convenient **fixed-dose combination regimen**. A strong recommendation (medium confidence).	The wording is satisfied. However, there is practically no combination of drugs in the Russian Federation.	**The 2016 WHO Guidelines, page 66** The use of an age-appropriate fixed-dose combination preparation is preferred for any regimen, if available.

Refusal to use stavudine **The only mention is on page 57.** Stavudine can only be used at a dosage of 30 mg 2 times a day.	It does not comply. Although stavudine is not included in the recommended regimens, there is no indication to stop using it.	**The 2016 WHO Guidelines, page 102** WHO recommends that the use of d4T-containing regimens be discontinued **Page 338** Programs should stop procuring... Stavudine (d4T): in light of the cumulative mitochondrial toxicity of d4T, it should no longer be procured, and people currently receiving d4T-based regimens should transition to a TDF-based regimen. (not mentioned at all in 2017 and 2018 editions)
Didanosine If it is not possible to use preferred and alternative regimens, it is recommended to use ARV drugs for special cases: NRTI: ddI - as an alternative to TDF or ABC drugs or AZT or phosphazide. Comments: The use of didanosine is not recommended... for more than 6 months in ART regimens due to the development of serious side effects associated with mitochondrial toxicity. **Page 28.** ddI is prescribed if TDF and ABC cannot be prescribed with hemoglobin <95 g/l, neutrophils <1000 cells/ml.	On September18, 2019, videx is excluded from the state register of drugs.	**The 2016 WHO Guidelines, page 338** Programs should stop: Didanosine (ddI): ddI should no longer be procured as it is no longer recommended as an alternative nucleoside reverse-transcriptase inhibitor (NRTI) in adult and adolescent second-line regimens due to toxicity, lower efficacy and inconvenient dosing requirements.
Using DTG It is included in an alternative first-line regimen **Page 26.** If it is not possible to use the preferred regimen, it is recommended to prescribe an alternative regimen:	It does not comply.	**The 2016 WHO Guidelines, page 3** DTG in combination with an NRTI backbone is recommended as the preferred first-line regimen for people living with HIV initiating ART: · Adults and adolescents; · Infants and children with approved DTG dosing (conditional recommendation, low-certainty evidence).
Using the EFV400 It is mentioned in comments only **Page 26.** EFV can be prescribed at a dose of 400 mg once a day, except for patients with tuberculosis, receiving tuberculostatics, and pregnant women (due to insufficient knowledge of the pharmacokinetics of the reduced dose in patients of these groups).	It does not comply, it is not included in the first-line regimen. This dosage is limited or not purchased in the RF.	**The 2016 WHO Guidelines, Page 3** Efavirenz at a low dose (EFV 400 mg) in combination with an NRTI backbone is recommended as the alternative first-line regimen for adults and adolescents living with HIV initiating ART(strong recommendation, moderate certainty evidence).
Recommendations for the use of dolutegravir in women of childbearing age and pregnant women Not specified.		**The 2016 WHO Guidelines, Page 3** Effective contraception should be offered to adult women... of childbearing age. DTG can be prescribed for adult women... if they have been fully informed of the potential increase in the risk of neural tube defects (at conception and until the end of the first trimester). If women identify pregnancy after the first trimester, DTG should be initiated.
First-line ART for special patient groups:		
Pregnant **Page 28** Prescription of preferred regimens (TDF and/or EFV) is not recommended. For pregnant women, ART is carried out in accordance with the Clinical Guidelines (Treatment Protocol) "HIV Infection: Prevention of Perinatal Transmission of Human Immunodeficiency Virus," 2017. They are not registered on the website of the Ministry of Health.	It does not comply.	**The 2016 WHO Guidelines, page 7** There is no specific regimen for pregnant women, but they should be fully informed of the potential increase in the risk of neural tube defects: TDF + 3TC (or FTC) + DTG.

Renal failure (creatinine clearance below 30 ml/min) **Page 28.** Preferred regimens (TDF and/or EFV) are not recommended, replace TDF with AZT or ABC.		Not highlighted separately TAF may be considered for people with established osteoporosis and/or impaired kidney function
Tuberculosis **Page 25.** Preferred regimens may also be prescribed for patients with active tuberculosis and chronic viral hepatitis B.		In active TB patients receiving rifampicin, all boosted PIs at standard doses are contraindicated due to drug interactions with rifampicin and a significant decrease in PI concentration in plasma
Hepatitis B **Page 25.** Preferred regimens may also be prescribed for patients with active tuberculosis and chronic hepatitis B		Preferred regimens include tenofovir
HIV-2 **Page 28.** Prescribing the preferred regimens (TDF and/or EFV) to patients is not recommended.		**The 2016 WHO Guidelines, page 290 (338)** In areas with a high prevalence of HIV-2 infection, the procurement and use of formulations with two-drug FDCs (TDF with 3TC, TDF with FTC and AZT with 3TC) might be a preferred option, as this provides the flexibility to combine the NRTI backbone with protease inhibitors (PIs) or integrase strand transfer inhibitors (INSTIs) in first- and second-line therapy for people living with HIV-2 infection.
Recommendations for breastfeeding of babies Not specified		Allowed if the mother receives ARV drugs
Monitoring before and after starting ART		

Before starting ART Approved by the standard (Order No. 796n) **Pages 36-37.** It is recommended to carry out the following diagnostic measures to make a decision to start ART as an urgent matter: · Determination of the clinical stage of the disease according to CR, 2006; · Determination of the CD4 count; · Pregnancy test. · It is recommended to conduct the following diagnostic measures to make a decision on the choice of ARVs: · Determination of serum creatinine level (GFR estimate) - when choosing TDF; · HLA B * 5701 screening- when choosing ABC; · Study of the level of hemoglobin and neutrophils - when choosing AZT, p-AZT; · Calculation of the CD4 count - when choosing EFV, NVP, RPV; · Study of the level of transaminases - when choosing NVP, EFV; · Study of the level of bilirubin and its fractions - when choosing an ATV; · Study of lipid profile - when choosing PI and EFV; · Identification of osteopenia or its high risk - when choosing TDF.	In general, it does not comply	**Before starting ART** CD4 cell count (every 6-12 months if ART initiation is delayed). Hemoglobin test for starting AZT Pregnancy test Blood pressure measurement Serum creatinine and estimated glomerular filtration rate (eGFR) or starting TDF Alanine aminotransferase for NVP Baseline CD4 cell count
After starting ART, clinical and laboratory examination should be performed three times monthly. Each time the doctor conducts history taking; physical examination; counseling on ART issues; assessment of adherence to ART (page 37). Laboratory: after 1 month VL; clinical blood test; ALT, AST, creatinine. After 2 months: VL (if during the 1st month of treatment, VL decreased by less than 10 times). After 3 months: VL, CD4 count; clinical blood test; ALT, AST, creatinine; general urine analysis. Further, every 3 months with an immune status above 500 and undetectable VL - every 6 months.	In general, RF recommendations are more complete.	**The 2016 WHO Guidelines, page 128** Serum creatinine and eGFR for TDF Pregnancy test, especially for women of childbearing age not receiving family planning and on treatment with DTG or low-dose EFV HIV viral load (at 6 months and 12 months after initiating ART and every 12 months thereafter) CD4 cell count every 6 months until patients are stable on ART
Recommendations for switching to second-line ART regimens, including special patient groups		

When in failure

Page 29. Switching to second-line ART is recommended after repeated (with an interval of no more than 4 weeks) detection of detectable VL levels after 6 months or more of ART in patients who have achieved virological efficacy.

The choice of the regimen depends on the first-line regimen.

ART first-line	ART second-line	
	Preferred	Alternative
TDF** + 3TC** or FTC	ABC** + 3TC** AZT** + 3TC**	ABC** + AZT** or pAZT** ddI** + AZT** or pAZT** ABC** + ddI**
ABC** + 3TC**	TDF** + 3TC** or FTC AZT** + 3TC**	TDF** + AZT** or pAZT** ddI** + AZT** or pAZT**
AZT** + 3TC** pAZT** + 3TC**	ABC** + 3TC** TDF** + 3TC** or FTC	ABC** + ddI** TDF** + ABC**
EFV**	DTG, ATV**/r**, LPV/r**, DRV/r**	FPV**/r**, SQV**/r**
NVP**	DTG, ATV**/r**, LPV/r**, DRV**/r**	FPV**/r**, SQV**/r**
ATV**/r**	EFV**, NVP**, DTG	LPV/r**, DRV**/r**, RPV/FTC/TDF**, ETR**
LPV/r**	EFV**, NVP**, DTG	ATV**/r**, DRV**/r**, RPV/FTC/TDF**, ETR**
DRV/r**	EFV**, NVP**, DTG	RAL**, RPV/FTC/TDF**, ETR**
DTG	EFV**, NVP**	ATV**/r**, LPV**/r**, DRV**/r**

WHO recommendations 2019:

Population	Failing first-line regimen	Preferred second-line regimen	Alternative second-line regimens
Adults and adolescentsa	TDFb + 3TC (or FTC) + DTG	AZT + 3TC + ATV/r (or LPV/r)	AZT + 3TC + DRV/r
	TDF + 3TC (or FTC) + EFV (or NVP)	AZT + 3TC + DTGc	AZT + 3TC + ATV/r (or LPV/r or DRV/r)
	AZT + 3TC + EFV (or NVP)	TDFb + 3TC (or FTC) + DTG	TDFb + 3TC (or FTC) + ATV/r (or LPV/r or DRV/r)
Children and infants	ABC + 3TC + DTG	AZT+ 3TC + LPV/r (or ATV/r)	AZT + 3TC + DRV/r
	ABC (or AZT) + 3TC + LPV/r	AZT (or ABC) + 3TC + DTG	AZT (or ABC) + 3TC + RAL
	ABC (or AZT) + 3TC + EFV	AZT (or ABC) + 3TC + DTG	AZT (or ABC) + 3TC + LPV/r (or ATV/r)
	AZT + 3TC + NVP	ABC + 3TC + DTG	ABC + 3TC + LPV/r (or ATV/rf or DRV/r)

With intolerance

Page 33. If intolerance to any ARVs develops, it is recommended to conduct corrective measures are if there is no effect, it should be replaced in accordance with the spectrum of side effects.

Recommendations for the third line of ARVs

Page 32. The greatest difficulties arise while developing third-line and subsequent-line ART regimens when the choice of effective drugs is significantly limited. The optimal treatment regimen is chosen taking into account individual characteristics, previous experience with ART, and resistance testing. In patients with multiple HIV resistance to ARV drugs, the optimal choice of therapy is to include new classes of ARV drugs (fusion inhibitors, CCR5 receptor inhibitors) in the ARV regimen. A number of drugs are approved (Order of the Ministry of Health of Russia, dated November 20, 2018, № 802n).	Due to the fact that the choice of the third-line regimen is too individual, there can be no specific recommendation.	**The 2016 WHO Guidelines, page 159 (207)** National programs should develop policies for third-line ART (conditional recommendation, low-quality evidence). · Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as INSTIs and second-generation NNRTIs and PIs (conditional recommendation, low-quality evidence). · Patients on a failing second-line regimen with no new ARV drug options should continue with a tolerated regimen (conditional recommendation, very low-quality evidence).
Barriers to accessing key drugs recommended by WHO, when they are available (e.g., no registration, on inclusion in the list of Vital and Essential Drugs or procurement lists, high price, etc.)		N/A
Efficacy criteria for ART **Page 29.** ART is considered effective if after 1 month VL decreases by 10 or more times, after 3 months of therapy - below 400 copies/ml, and after 6 months - less than 50 copies/ml. **Virological failure criteria** **Page 29.** Repeated (with an interval of 2-4 weeks) detection of detectable VL levels (above 50 copies/ml) after 6 or more months of ART in patients with achieved virological suppression.		**The 2016 WHO Guidelines, page 129** **Efficacy criteria for ART** Not specified. **Viral failure** is defined by a persistently detectable viral load exceeding 1000 copies/ml (that is, two consecutive viral load measurements within a 3-month interval, with adherence support between measurements) after at least 6 months of starting a new ART regimen.
Part 5. Prevention and treatment of concomitant infections and diseases		
Recommendations for the prevention and treatment of co-infections, primarily (but not limited to): · HIV/viral hepatitis C (HCV) is absent; · HIV/HBV, mentioning ART prescription is on a priority basis; · HIV/TB - page 22: If a patient is diagnosed with active tuberculosis, treatment should be started, and then ART should be added: if the CD4 count is less than 50 cells/mm3 - within 2 weeks; with CD4 more than 50 cells/mm3- no later than after 8 weeks.	Both recommendations do not pay enough attention to this.	**The 2016 WHO Guidelines, page 147 (195)** Potential drug interactions should be considered when using ARV drugs and DAAs for HCV infection **WHO 2016, page 38** Xpert MTB/RIF should be used rather than conventional microscopy, culture, and drug susceptibility testing (DST) as the initial diagnostic test in adults and children suspected of having HIV-associated TB or multidrug-resistant TB. TB patients with known positive HIV status and TB patients living in HIV-prevalent settings should receive at least 6 months of a rifampicin-containing treatment regimen. The optimal dosing frequency is daily during the intensive and continuation phases

Prevention and treatment of opportunists **Page 32.** It is recommended to use prophylactic regimens of anti-tuberculosis drugs with CD4 counts less than 350 cells/mm3 for primary prevention of tuberculosis. A strong recommendation (high confidence). Comments: Primary tuberculosis prophylaxis is carried out in accordance with the current regulatory documents (currently, "Instruction on the chemoprophylaxis of tuberculosis in adults with HIV infection," approved on March 14, 2016). **Page 32.** Primary prophylaxis for pneumocystis pneumonia (PCP) and toxoplasmosis is recommended if CD4 counts are less than 200 cells/mm3 (less than 14%). A strong recommendation (high confidence). Comments: prophylaxis is conducted with co-trimoxazole 800 + 160 mg/day 3 times a week or 400 + 80 mg/day daily (until CD4> 200 cells/mm3 and undetectable HIV VL for more than 3 months). **Page 32.** It is recommended to carry out prophylaxis of non-tuberculous mycobacteriosis (M. avium complex, M. genavense, M. kansasii) with a CD4 count of fewer than 50 cells/mm3. A strong recommendation (high confidence). Comments: prophylaxis is conducted with one of the regimens until CD4> 100 cells/mm3 and undetectable HIV VL for more than 3 months are achieved: azithromycin 1200-1250 mg/week or clarithromycin 2 × 500 mg/day or rifabutin 300 mg/day.	Indications for co-trimoxazole prophylaxis vary. Most likely, it is worth leaving the indications for Russia as in Europe.	**The 2016 WHO Guidelines** Co-trimoxazole prophylaxis is recommended for adults (including pregnant women) with severe or advanced HIV clinical disease (WHO stage 3 or 4) and/or with a CD4 count ≤350 cells/mm3...
Prevention and treatment of relevant non-communicable diseases: · Cardiovascular diseases · Depression · Diseases of the central nervous system · Kidney diseases · Substance use. It is mentioned that ART may be delayed because of mental illness and severe drug dependence. Weak recommendation (low confidence). Comments: In these cases, it is assumed that it is impossible to form the required level of adherence to the therapy, and therefore ART can be postponed until recovery, remission, effective rehabilitation, and increased adherence.	The Russian guidelines do not pay attention to comorbidity.	**The 2016 WHO Guidelines, page 216 (264)** Assessment and management of cardiovascular risk should be provided for all individuals living with HIV according to standard protocols recommended for the general population (conditional recommendation, very low-quality evidence). **The 2016 WHO Guidelines, page 219 (267)** Assessment and management of depression should be included in the package of HIV care services for all individuals living with HIV (conditional recommendation, very low-quality evidence). **The 2016 WHO Guidelines, page 221 (269)** WHO, the United Nations Office on Drugs and Crime (UNODC) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) recommend a comprehensive package of nine interventions for HIV prevention, treatment and care for people who inject drugs; these are needle and syringe programs, OST, HIV testing and counseling, ART, preventing and treating STIs, condom programs, targeted behavior change communication, preventing and treating viral hepatitis and preventing, diagnosing and treating TB.
Other, not specified above.		

Part 6. Health service provision		
The provision of health services, including but not limited to: • Recommendations for the decentralization of services. • Recommendations for redistribution and delegation of services. • Recommendations for integration of services.	This is not mentioned in the Clinical Guidelines of the Russian Federation, nevertheless, some of these measures are taken with more or less success. And this is definitely a useful undertaking.	**The 2016 WHO Guidelines, page 45** Decentralization of HIV treatment and care should be considered as a way to increase access to and improve retention in care: • initiation of ART in hospitals with the maintenance of ART in peripheral health facilities (strong recommendation, low-quality evidence); • initiation and maintenance of ART in peripheral health facilities (strong recommendation, low-quality evidence); • initiation of ART at peripheral health facilities with maintenance at the community level (strong recommendation, moderate-quality evidence). Trained and supervised lay providers can distribute ART to adults, adolescents and children living with HIV (strong recommendation, low-quality evidence). Trained non-physician clinicians, midwives and nurses can initiate first-line ART (strong recommendation, moderate-quality evidence). Trained non-physician clinicians, midwives and nurses can maintain ART (strong recommendation, moderate-quality evidence). Trained and supervised community health workers can dispense ART between regular clinical visits (strong recommendation, moderate-quality evidence).

Romania

Part 1. Basic information	
Name of the current version of document and the and a link to it.	As the National Romanian HIV guidelines was not updated since 2014, the local recommendations were to use the EACS guidelines 2016 (translated into Romanian and adapted to the National conditions and availabilities). It is expected that on beginning of 2020, will be created a version of the EACS 2019 guidelines, adapted to the local conditions.
Year of the current version	N/A
No. of the normative document defining the status of these recommendations (order, resolution, if applicable).	N/A
Legal status of recommendations: mandatory or advisory in nature, what additional documents govern the need for recommendations.	No legal document (according to the expert knowledge).
Frequency of the document revision (is it defined? by which documents is it regulated?).	HIV National guideline exist but not revised since 2013- 2014 and it is not in use. There is no regulatory document. It was decided to use the EACS guideline (adapted).
Level of evidence (description of the applicable system).	N/A
Members of the editorial board (are representatives of NGOs/patient organizations included?).	N/A
List and brief description of documents additionally regulating the use of ARVs in the country, including the following documents, but not limited to: • laws governing the nature of supplying the ARVs (free of charge/ paid, by prepaid medical care plan or at the expense of a special national program, etc.); • lists of Vital and Essential Drugs; • lists of drugs to be procured at the expense of different budgets; • treatment standards, etc.	Antiretroviral treatment in Romania is free of charge. There is a HIV National Program of the Romanian Ministry of Health. PEP is reimbursed by the National HIV Program, PrEP is not. **List of essential drugs:** NRTIs: ZDV, 3TC, FTC, ABC, TDF, ABC + 3TC (Kivexa), TDF/ FTC (Truvada), TAF/ FTC (Descovy). NNRTIs: EFV, ETR, NVP, RPV. PIs: ATV, DRV, LPV/r. INSTI: DTG, RAL. CCR5-receptor antagonist: MVC. FDCs: ABC/ 3TC/ DTG (Triumeq), TAF/ FTC/ EVG/ COBI (Genvoya). **Drugs not available or not registered in Romania:** NNRTI: Doravirine. INSTI: Bictegravir. FDCs: TDF/ FTC/ RPV (Eviplera, Complera), TDF/ 3TC/ DOR (Delstrigo), TDF/ FTC/ DRV/c (Symtuza). TB treatment is provided for free through the TB National program. Bedaquiline and capreomycine were available only due to external funds (Norwegian funds).

Page and quote from national protocols	Comment	Link to relevant WHO recommendation, page, document, quote
Part 2. Guidelines for diagnostics		
Retesting before inclusion in care and treatment programs	Yes.	
Pre-test and post-test advising services.	Yes.	
Testing by non-professional medical workers using express diagnostic methods.	Some rapid diagnostic tests for HIV and HCV are used by physician working at NGOs, in prisons, OST centers or GPs in private practices (especially for people belonging to key populations). Rapid tests are used also by social workers from National NGOs (CARUSEL, ARAS), to test people from hard-to-reach groups, homeless, people who inject drugs, MSM etc.) After the initial positive test, subjects are sent to the infectious diseases' hospital (from the HIV regional centers) to be confirmed and treated. HIV testing for all pregnant women, patients diagnosed with TB or with sexually transmit-ted diseases is mandatory in Romania.	

Testing initiated by a medical worker.	Yes, medical worker or social worker from NGOs working, working with persons from key populations.	
Diagnosis of HIV infection in children and infants, in particular, the sensitivity and specificity of tests.	All the infants born to HIV infected mothers are tested for HIV-RNA. Use of HIV-RNA (if negative), repeated after 2 months of age (ART prophylaxis is ended). Usually 3 negative HIV-VL are performed to have a final diagnosis (or not infected).	
Testing in special groups (adolescents, pregnant women, couples and partners).	Testing for pregnant women, patients with TB and STIs, partners of HIV positive patients, PWIDs is mandatory. We recommend testing also for MSM, sex workers, homeless and patients with some signs/symptoms that can be suggestive for HIV (neurological signs - focal lesions, dermatological signs - thrush, molluscum contagiosum, herpes zoster etc., unexplained fever, weight loss or diarrhea, hematological abnormalities (unexplained anemia, leucopenia, thrombocytopenia) etc.	
Diagnostic algorithms	2 ELISA tests from different blood samples (HIV antibodies positive), confirmed by HIV VL.	
Part 3. ARVs for HIV prevention		
Pre-exposure prophylaxis of HIV infection.	PrEP not reimbursed by the National HIV program.	
Algorithm and regimens of post-exposure prophylaxis for different population groups, including for PMTCT.	As backbone TDF + FTC or AZT + 3TC (alternative). The third drug is usually a PI (mainly LPV/r or DRV/r) or RAL. In special circumstances, when the choice is an INSTI, RAL or DTG can be used. DTG is still not the first option for PEP because of cost issues (no generic formulation for DTG available in Romania). **Algorithm for PMTCT** If the woman is undetectable during pregnancy and at delivery, only AZT is recommended for 4 weeks (with careful monitoring of hemoglobin). In case of a woman diagnosed in late pregnancy or after delivery, the recommendation is for AZT + 3TC + NVP or AZT + NVP.	Discordant with WHO (2016), page 34, recommendation for use of DTG as third agent for PEP.
Part 4. Antiretroviral therapy regimens		
When ART should be started, including recommendations for specific groups of patients (for whom urgent indication is recommended).	ART is recommended in all HIV positive patients, irrespective of the CD4 cell count. If the patient is a late presenter or with advanced HIV disease, ART is initiated urgently (except in patients with central nervous system opportunistic infections, crypto- or TB meningitis, when the treatment of the OIs is initiated first to prevent life-threatening IRIS). Treatment initiation is urgent in HIV pregnant women to prevent MTCT.	Concordance with WHO.
Choosing the Line 1 drugs, including:	TDF + 3TC (FTC) + DTG (RAL) is recommended as first line regimen.	Concordant with WHO (page 3 and 7 of the updated WHO treatment guidelines July 2019) for the use of DTG as first line regimen.
· Preferences for fixed dose combination (FDCs) drugs.	There are only 2 FDC available in Romania: ABC/3TC/DTG (Triumeq) and TAF/FTC/ELV/COBI (Genvoya).	
· Refusal to use stavudine.	d4T – not in use.	

• Use of DTG and EFV400 in accordance with the updated recommendations (2018, 2019).	EFV 400 mg is not recommended as an alternative. RAL is not used in small children (not available dispersible form or tablets of 100 mg), DTG not available for small children.	Discordance in use of EFV 400mg as alternative regimen.
• Recommendations for use of dolutegravir in women of childbearing age and pregnant women.	DTG can be used in women of childbearing age, especially if they use contraception and/or they receive full, updated information about the risk of neural tube defects (reduced) in the newborn, if under DTG during conception.	
	In HIV pregnant women, DTG is usually not recommended. In HIV pregnant women the first recommendation for the third agent is RAL.	Discordant with WHO guidelines (July 2019).
	If the woman is diagnosed in late pregnancy, DTG can be continued.	Concordant with WHO guidelines (updated version July 2019).
	EFV is **not recommended usually** as first line in HIV pregnant women.	Discordant with WHO guidelines (EFV recommended).
Line 1 ART for special patient groups.	For PWIDs – special attention if they are under substitution therapy with methadone (drug-drug interactions, for example with EFV). Patients with HIV/HCV co-infection treated with DAAs (check for drug-drug interactions with ART). Patients with malignancies – drug-drug interactions with PIs. In patients with multiple comorbidities INSTI are recommended in order to reduce the risk of DDIs, not to increase CVD risk (avoid ABC and PIs) etc.	
Recommendations for breastfeeding of babies.	Breastfeeding is not recommended for HIV positive mothers in Romania, even if undetectable under ART. Formula feeding is indicated.	
Monitoring before and after starting ART.	**All patients are monitored before starting ART for:** • Hematology, liver and renal function (eGFR), glucose, lipids. • ECG, blood pressure. • Weight, height. • CD4 cell count (%), CD8 (%), CD4/CD8, HIV VL, HLA-B-5701. • Screening for TB, hepatitis [B (D), C], syphilis, CMV, toxoplasma (in some clinics screen also for HTLV 1, 2) • The PAP smear is not performed in every HIV clinic. • Framingham score, FRAX – performed only in some clinics. **Monitoring after starting ART:** • CD4, CD8: every 3-4 months. • HIV-VL: every 6 months. • In special circumstances (pregnancy, lack of adherence etc.), monitoring can be more frequent. • In patients belonging to risk groups (PWIDs, MSM) screening for hepatitis B, C, syphilis - every year.	

<table>
<tr><td>Recommendations for switching to Line 2 ART regimens, including for special patient groups, including the preferred alternative regimen.</td><td>In case of toxicities, viral resistance, simplification, drug- drug interactions.

The preferred alternative regimen depends on the circumstances (e.g., patient with tubular nephropathy or Fanconi syndrome are switched from TDF, patient with CVD risk switched from ABC or PIs etc.)

Lack of response to the first line regimen
<table><tr><th>Line 1 regimen</th><th>2nd line regimen</th><th>Alternative 2nd line</th></tr><tr><td>TDF + FTC + DTG</td><td>ABC + 3TC/ TDF + DRV/r</td><td>ABC + 3TC/ TDF+ ATV/r</td></tr><tr><td>TDF + FTC (3TC) + EFV</td><td>ABC + TDF (3TC) + DTG</td><td>ABC + 3TC (TDF) + RAL or DRV/r</td></tr><tr><td>ABC + 3TC + EFV or PIs</td><td>TDF + FTC + DTG</td><td></td></tr></table>
AZT is rarely recommended as part of backbone regimen in Romania (due to toxicity), except special circumstances and PMTCT.

There are differences with the WHO recommendation for the second line regimen.</td><td></td></tr>
<tr><td>Recommendations for Line 3 ARVs.</td><td>3rd line regimen is usually recommended after the genotyping resistance test is performed.</td><td></td></tr>
<tr><td>Barriers to accessing key drugs recommended by WHO, when they are available (e.g., no registration, no inclusion in the list of Vital and Essential Drugs or procurement lists, high price, etc.)</td><td>DTG not used for PEP, high cost; DTG generic is not available

EFV 400 mg is not recommended as an alternative (not registered for this dosage)

Pediatric formulations for DTG and RAL (dispersible) are not available in Romania

AZT is rarely used in Romania (due to toxicity), except for PMTCT and other special circumstances</td><td>N/A</td></tr>
<tr><td colspan="3">Part 5. Prevention and treatment of co-infections and co-morbidities</td></tr>
<tr><td colspan="3">Recommendations for the prevention and treatment of co-infections, primarily (but not limited to):</td></tr>
<tr><td>· HIV/Viral Hepatitis C (HCV);</td><td>INSTI preferred, taking in consideration the lack of drug-drug interactions with DAAs.</td><td></td></tr>
<tr><td>· HIV/HBV;</td><td>TDF/TAF + FTC/3TC are used as a backbone in all HIV/HBV co-infected patients.</td><td></td></tr>
<tr><td>· HIV/TB.</td><td>If the anti-TB regimen contains RIF: EFV is recommended in patients that are not previous experienced or resistant to EFV, RAL 800 mg x2 or DTG (50 mg x 2).</td><td>Concordance with WHO guidelines.</td></tr>
<tr><td>· Prevention and treatment of relevant noncommunicable diseases:</td><td></td><td></td></tr>
<tr><td>· Cardiovascular diseases;</td><td>Avoid ABC, PIs (DRV/r, LPV/r), preferred INSTI (RAL, DTG).</td><td></td></tr>
<tr><td>· Depression;</td><td>Avoid EFV, evaluate careful about DTG, use depression scale.</td><td></td></tr>
<tr><td>· Diseases of the central nervous system;</td><td>Depends if CNS opportunistic infections (crypto, TB meningitis), CNS malignancies, HAND.</td><td></td></tr>
<tr><td>· Kidney diseases;</td><td>Avoid TDF if eGFR < 60 or TAF if eGFR < 30.</td><td></td></tr>
<tr><td>· Substance use.</td><td>Check for DDIs if substitution therapy with methadone, check for hepatitis B, C.</td><td></td></tr>
<tr><td>Other points not mentioned above.</td><td>Bone disease, risk of fractures, frailty.</td><td></td></tr>
</table>

Part 6. Provision of health services		
The provision of health services, including but not limited to: • Recommendations for decentralization of services. • Recommendations for redistribution and delegation of services. • Recommendations for integration of services.	**Recommendations for redistribution and delegation of services:** Taking in consideration the new pan-genotypic DAAs for HCV treatment with good tolerability, lack of adverse events and drug-drug interactions (with INSTI), treatment for HCV could be prescribed and monitored in the future by GPs. **Recommendations for integration of services:** TB and HIV are treated in Romania in infectious diseases hospitals or in TB hospitals, depending on the HIV center or region (in order to ensure the best conditions for the isolation of the HIV/TB co-patients) There is one integrated HIV and OST center in Bucharest. **Recommendation:** For PWIDs it would be preferable to have an integrated HIV/TB, HIV/hepatitis (HBV, HCV) and OST center. Patient should be treated and evaluated for HIV, TB, HCV, HBV and to have the possibility to receive opioid substitution at the same center.	
Part 7. Other clinically significant discrepancies that do not fall within the thematic blocks above		
Other clinically significant discrepancies that the experts are aware of, between the WHO recommendations for the diagnosis and use of antiretroviral drugs and national recommendations, for example, in the part of providing harm reduction services for patients who use psychoactive substances, etc.	No major discrepancies in the use of ART in naïve patients. In Romania there is a lack of harm reduction services, especially after the decrease in the external funding (Global fund). Lack of needle-exchange services and insufficient methadone procurement compared to the local needs in former PWIDs. HIV prevention programs and funds are still insufficient in Romania.	

Serbia

Part 1. Basic information	
Name of the current version of document and a link to it.	EACS guidelines 10.0
Year of the current version.	2019
No. of the normative document defining the status of these recommendations (order, resolution, if applicable).	N.A
Legal status of recommendations: mandatory or advisory in nature, what additional documents govern the need for recommendations.	Advisory.
Frequency of the document revision (is it defined? by which documents is it regulated?).	No official recommendations nor regulations about the necessity of national guidelines for HIV treatment.
Level of evidence (description of the applicable system).	
Members of the editorial board (are representatives of NGOs/patient organizations included?).	Physicians treating HIV. No representatives of Serbian NGOs/patient organizations.
List and brief description of documents additionally regulating the use of ARVs in the country, including the following documents, but not limited to: · laws governing the nature of supplying the ARVs (free of charge/ paid, by prepaid medical care plan or at the expense of a special national program, etc.); · lists of Vital and Essential Drugs; · lists of drugs to be procured at the expense of different budgets; · treatment standards, etc.	Policy on list of medications prescribed and issued on the expense of mandatory health insurance All ARV are on the List A – medications issued on the basis of physicians' prescription these documents ensure that all ARV are free of charge for all patients who have prescription from an infectologist treating HIV.
Other relevant information	At this moment there are no official National HIV treatment guidelines in Serbia. One of the activities planned by the Strategy for prevention and treatment of HIV infection and AIDS in Republic of Serbia, 2018-2025 is writing National guidelines for treatment. In the meantime, there is general consensus between HIV physicians achieved at an assembly in 2011 that Serbia should follow EACS guidelines. The latest version of EACS guidelines translated into Serbian are from 2014 but physicians use the EACS 10.0 for guidance in treating HIV.

Page and quote from national protocols	Comment	Link to relevant WHO recommendation, page, document, quote
Part 2. Guidelines for diagnostics		
Retesting before inclusion in care and treatment programs.	Retesting is obligatory before starting ART.	WHO 2016 guidelines. 2. HIV diagnosis
Pre-test and post-test advising services. Strategy for prevention and treatment of HIV infection and AIDS in Republic of Serbia, 2018-2025. Chapter 3.2.1.	There are many VCT centers in Serbia which offer pre- and post-testing advising services. Most of newly discovered HIV infections come from VCT centers.	WHO 2016 guidelines. 2.3 Pre- and post-test services
Testing by non-professional medical workers using express diagnostic methods. Strategy for prevention and treatment of HIV infection and AIDS in Republic of Serbia, 2018-2025. Chapter 3.2.	There are rapid test sites in Novi Sad and Belgrade, and soon in Kragujevac. They are provided by NGO in collaboration with national health service institutions.	WHO 2016 guidelines. 2.4 Principles and approaches for service delivery
Testing initiated by a medical worker. Strategy for prevention and treatment of HIV infection and AIDS in Republic of Serbia, 2018-2025. Chapter 3.2.	HIV testing could be provided by any medical worker with the consent of the person tested – "opt in".	

Diagnosis of HIV infection in children and infants, in particular, the sensitivity and specificity of tests. https://www.chiva.org.uk HIV testing guidelines for children of HIV positive parents and/or siblings in the UK and Ireland	Testing of children suspected to have HIV needs to be consented by their parents. Testing of infants is done only in the symptomatic infants. Testing of infants is done by the protocol provided by CHIVA and WHO.	WHO 2016 guidelines. 2.5 HIV diagnosis in infants and children
Testing in special groups (adolescents, pregnant women, couples and partners). Strategy for prevention and treatment of HIV infection and AIDS in Republic of Serbia, 2018-2025. Chapter 3.2.	Pregnant women are not routinely tested for HIV. Routine HIV testing for pregnant women is encouraged by the latest National strategy for HIV/AIDS.	
Diagnostic algorithms (WHO 2016) for low-prevalence settings. In settings with less than 5% HIV prevalence in the population tested, a diagnosis of HIV positive should be provided to people with three sequential reactive tests.	Two antibody test from different specimens, then a WB test; alternatively, a PCR HIV test might be done as a confirmatory test (qualitative PCR HIV is available from National health services, while quantitative PCR HIV is available only in HIV treatment centers – infectious diseases clinics).	
Other points not mentioned above.	Most of the points mentioned above are only partially done in practice but are planned by the Strategy for prevention and treatment of HIV infection and AIDS in Republic of Serbia, 2018-2025. The strategy was made in compliance by, among others, WHO guidelines.	
Part 3. ARVs for HIV prevention		
Strategy for prevention and treatment of HIV infection and AIDS in Republic of Serbia, 2018-2025	PrEP is available in pharmacies as a generic drug. It is not covered by health insurance but the price of the generic drug was reduced earlier this year. There are no PrEP services in public hospitals. PrEP is mentioned in the latest version of the National HIV/AIDS strategy as one of the key points of future development.	WHO 2016 guidelines. 3.1 Oral pre-exposure prophylaxis for preventing the acquisition of HIV
Algorithm and regimens of post-exposure prophylaxis for different population groups, including for PMTCT (based on both WHO and EACS guidelines): 1. Risk assessment. 2. Testing for HIV, HBV, HCV. 3. PEP regimens: TDF/FTC + RAL, or + DRV/r, or + DTG, or LPV/r.	PEP is not covered by the health insurance except for infants born to HIV+ mothers. PEP is prescribed by the HIV physician; the medications might be bought by the person in risk of acquiring HIV or might be provided by the HIV physicians.	WHO 2016 guidelines. 3.2 Post-exposure prophylaxis
Other points not mentioned above.	Guidance for diagnostic of HIV, including ARV for prevention was defined in National strategies for HIV/AIDS in 2011 and in the latest National strategy published in 2019. Both strategies are in compliance with WHO recommendations for testing and preventing HIV.	
Part 4. Antiretroviral therapy regimens		
ART is recommended to all adult PLWH irrespective of CD4 count.	This recommendation is accepted and applied in practice. The only reason for not starting ART is patient's unwillingness to start. Genotype testing is not routinely done before ART initiation. It's available on a special request. Rapid, same date ART initiation is not done.	„ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count" (WHO 2016 guidelines. 4.3 When to start ART).

Preferred: **2NRTI+INSTI** ABC/3TC+DTG; ABC/3TC/DTG; TAF/FTC or TDF/FTC or TDF/3TC + DTG; TAF/FTC/BIC; TAF/FTC or TDF/FTC or TDF/3TC + RAL. **Alternative:** **2NRTI+INSTI** ABC/3TC + RAL qd or bid; TDF/FTC/EVG/c; TAF/FTC/EVG/c. **2NRTIs + NNRTI** ABC/3TC +EFV; TAF/FTC or TDF/FTC or TDF/3TC + EFV TDF/FTC/EFV. **2 NRTIs + PI/r or PI/c** ABC/3TC + ATV/c or ATV/r; ABC/3TC + DRV/c or DRV/r; TAF/FTC or TDF/FTC or TDF/3TC + ATV/c or ATV/r.	• DTG alone should be given only as a second line drug according to Republic Fond for Health Insurance. • ABC/3TC/DTG as a single tablet regiment (Triumeq) can be given in the first line treatment. • TAF is not available in any form in Serbia. • BIC is not available in Serbia (there are indications single tablet regimen TAF/FTC/BIC should be available in 2020.) • TDF/FTC/EFV is not available as a single tablet regimen. • ATV/c and ATV/r are not available in Serbia. • There is no official recommendation for preferences towards single tablet regiments. • Although there is no official document Stavudine is not used in any patients. • EFV in 400mg dose is not given since there is no TDM which is recommended by EACS.	Update of recommendation on first- and second- line antiretroviral regiments, WHO, 2019.
Treatment of Pregnant Women Living with HIV or Women Considering Pregnancy 1. 1Women planning to be pregnant or becoming pregnant while already on ART: Maintain ART, unless taking DTG. 2. Women becoming pregnant while treatment-naïve: Starting ART as soon as possible is highly recommended. 3. Women whose follow-up starts late in the second or in the third trimester: Start ART immediately and consider RAL or DTG as the preferred choice to obtain rapid HIV VL decline and to ensure the HIV VL is undetectable by the time of delivery. 4. Women whose HIV VL is not undetectable at third trimester: Perform resistance testing and consider changing to or adding INSTI. 5. Women whose HIV VL is > 50 copies/mL at week 34-36 of pregnancy: Elective cesarean section to be planned at week 38 + iv ZDV. 6. Women diagnosed with HIV in labour: Cesarean section + iv ZDV.	• DTG may be given to women in childbearing age and there is no official consent form for this situation. • Pregnant women are started on ART ASAP (but there is no universal screening on HIV in pregnancy). • Resistance testing in general is problematic due to in-house methods and long lag time until results are available. • intravenous ZDV is not available. • PEP for newborns is limited to AZT, 3TC and LPV/r (the only medication available in syrups or granules).	Update of recommendation on first- and second- line antiretroviral regiments, WHO, 2019.
We advise against breastfeeding.	This recommendation is fully applied in daily practice and HIV+ women are discouraged from breastfeeding	WHO 2016 guidelines. 4.4.8 Infant feeding in the context of HIV.

Assessment of PLWH at Initial & Subsequent Visits **HIV disease:** Plasma HIV-VL prior to initiation and then every 3-6 months. Genotypic resistance test and sub-type R5 tropism (if available). CD4 absolute count and %, CD4/CD8 ratio (optional: CD8 and %). HLA-B*57:01. **Coinfections. STD:** Initially, annualy, if indicated. **TB:** PPD, CXR initially. IGRA (in high risk groups). **Others:** VZV, measles, toxoplasma, CMV serology. **Comorbidities:** FBC, BMI, Framingham score, BP, lipids, glucose, ALT, AST, AL, bilirubin, urin, bone profile. Depression questionnaire. Cancers.	• Plasma HIV VL is available in treatment centers in Serbia (in some regularly, in some occasionally); efforts are being made to improve this service. • genotypic resistance is done in failing patients with VL above 1000 copies/mL; resistance is done in one center which requires efforts to send the specimen and the results are sometimes long overdue. • R5 tropism is available in failing patients. • HLA testing is available for all patients initiating ART. • CD4, CD4/CD8, CD8 are done in all treatment centers (in some there are issues regarding old counters and lack of reagents). • Testing for STDs is done routinely before initiating ART. • Annual STD testing is not a routine in all treatment centers. • Testing for HBV and HCV is a part of a routine assessment before starting ART (HEV, HDV are not done routinely). • CXR is routinely done. • IGRA and PPD are not routinely done but could be done on demand. • VZV, Toxo, CMV, EBV and HSV serology are routine. • Screening for comorbidities is routinely done before initiation and annually. • Anal HPV smears are unavailable.	WHO 2016 guidelines. 4.5 Monitoring the response to ART and diagosing treatment failure.
Management of virological failure (VF) Evaluate adherence, tolerability, drug-drug interactions, drug-food interactions, psychosocial issues. Perform resistance testing on failing therapy (usually routinely available for HIV VL levels >200-500 copies/mL and in specialized laboratories for lower levels of viraemia) and obtain historical resistance testing for archived mutations. Tropism testing if considering MVC. Consider TDM. Review ART history. Identify treatment options, active and potentially active drugs/combinations. Use at least 2 and preferably 3 active drugs in the new regimen (including active drugs from previously used classes). Any regimen should use at least 1 fully active PI/b (e.g. DRV/r) plus 1 drug from a class not used previously e.g. INSTI, FI, or CCR5 antagonist (if tropism test shows R5 virus only), or 1 NNRTI (e.g. ETV), assessed by genotypic testing. Alternatively, a regimen can be constructed with DTG (when fully active) plus 2 NRTIs, of which at least 1 NRTI is fully active.	• Resistance testing on failing therapy is done only in samples with HIV-VL above 1000 copies/mL. • Due to restrains in resistance testing we use at least two new antivirals one of them being an antiviral high genetic barrier - either DTG (in DTG naive) or PI based ART (DRV/c or DRV/r).	Update of recommendation on first- and second- line antiretroviral regiments, WHO, 2019.

Recommendations for Line 3 ARVs. N/A	Highly experienced patients have resistance test done (they comprise most of the patients who have resistant testing – ART is then based on the results of the test.	Update of recommendation on first- and second- line antiretroviral regiments, WHO, 2019.
Barriers to accessing key drugs recommended by WHO, when they are available (e.g., no registration, no inclusion in the list of Vital and Essential Drugs or procurement lists, high price, etc.)	N/A	N/A
Other points not mentioned above.		
Part 5. Prevention and treatment of co-infections and co-morbidities		
Recommendations for the prevention and treatment HIV/HCV · Substitution therapy (opioid replacement therapy) in persons with active drug use as a step towards cessation of active drug use should be encouraged. · Every person with HCV/HIV co-infection must be considered for DAA-based anti-HCV treatment regardless of liver fibrosis stage. · Due to similar HCV cure rates and tolerability in HCV/HIV co-infected persons as in HCV mono-infected persons under DAA therapy, treatment indication and regimens are to be the same as in HCV mono- infection.	· Substitution therapy (opioid replacement therapy) is available and implemented. · Treatment of HIV/HCV co-infection is very problematic. · HCV medications are not available for PLWH except in late stages of liver damage (treatment is available for limited number of patients. · National committee decides medication distribution and HIV coinfection has no priority to HCV monoinfected patients; the decision is based on liver damage assessed using elastography or liver biopsy). · HCV and HIV/HCV patients might get generic HCV medications from other countries at their own expense and risk but are followed up in hepatitis clinics.	WHO 2016 guidelines. 5. Prevention, screening and management of common coinfections and comorbidities.
Recommendations for the prevention and treatment HIV/HBV Vaccinate if seronegative. Repeat doses until anti-HBs antibodies ≥100 IU/L. All PLWH with HBV/HIV co-infection should receive ART that includes TDF or TAF unless history of tenofovir intolerance. Stopping anti-HBV active ART should be avoided.	Recommendations for HIV/HBV co infection are fully implemented in daily practice.	
Recommendations for the prevention and treatment HIV/TB **Initial phase:** Rifampicin + isoniazid + pyrazinamide + ethambutol (weight based). **Alternative:** Rifambutin + isoniazid + pyrazinamide + ethambutol (weight based). **Continuation phase:** Rifampicin/rifabutin + isoniazid.	· Prevention of TB with isoniazid is not routinely recommended. · Rifambutin is not available in Serbia.	
Prevention and treatment of comorbidities Lifestyle changes (dietary counseling, exercise promotion, smoking cessation).	HIVAS (HIV association in Serbia) has put as one of priorities building a team of non-HIV specialist to help treat comorbidities in PLWH; due to high stigma levels among physicians this is an imperative.	WHO 2016 guidelines. 5.3.1 Assesment and management of non-communicable diseases 5.3.2 Assesment and management of depression.
Prevention and treatment of cardiovascular diseases Assessing CVD risk (annually) - use the Framingham equation or whatever system local National Guidance recommends. Advise on diet, switching ART if the 10 year CVD risk is above 10%. Identifying and correcting modifiable risk factors (BP, coagulation, DM, lipids).	· Framingham equation is widely used for CVD risk assessment. · Correction of risk factors such as high BP, DM or lipids is sometime done by the HIV specialist but other specialist (cardiologist, endocrinologist might be included).	

Prevention and treatment of depression Screening of all PLWH recommended in view of the high prevalence of depression Screen every 1-2 years. Treatment of depression: Mild - Problem-focused consultation, consider antidepressant treatment, recommend physical activity; Intermediate – start antidepressant treatment; Severe – refer to expert.	• There is no routine screening for depression. • When diagnosed depression is mostly treated by psychiatrist. • Antidepressants cannot be prescribed by an HIV physician. • Psychotherapy is available in only in some HIV centers.	
Prevention and treatment of kidney disease Annual risk assessment (risk factors hypertension, diabetes, CVD, family history, viral hepatitis, low current CD4 count, smoking, older age, concomitant nephrotoxic drugs); eGFR; urine dipstick. Treatment of kidney disease: Check risk factors for CKD and nephrotoxic medicines including ART; Discontinue or adjust drug dosages where appropriate.	• Kidney disease assessment (creatinine, urea, urine) are a part of annual check. • Nephrologists are consulted in the case when kidney disease is diagnosed.	
Prevention and treatment of substance abuse Opioid substitution therapy (methadone, buprenorphine). Needle exchange programs.	OST and needle exchange programs are available in Serbia.	
Other points not mentioned above.	Serbian HIV association has made multidisciplinary approach to HIV one of its priorities. The aim is to bring together a group of non-HIV specialist trained in HIV to help manage HIV comorbidities.	
Part 6. Provision of health services		
Strategy for prevention and treatment of HIV infection and AIDS in Republic of Serbia, 2018-2025 Four HIV centers in Serbia since 2008.	All four centers are running well. Decentralization has been fully successful.	

Tajikistan

Part 1. Basic information	
Name of the current version of the document and the link to it.	"Guidelines for the diagnosis, monitoring, and treatment of HIV infection in Tajikistan" (newborns, children, adolescents, and adults) dated May 14, 2019, No. 342 Code of Health Care, dated May 30, 2017, No. 1413 "Order of the Ministry of Health and Social Protection of the Population of the Republic of Tajikistan (the MHSPPRT), dated September 03, 2009, No. 597 "Manual on the prevention of HIV transmission at the workplace" Government Resolution on "Procedure for medical examination," No. 528 dated August 06, 2014 "Order of the MHSPPRT, dated September 30, 2015, No. 832 "On permission to conduct HIV testing among UGP on the basis of public organizations"
Year of the current version.	May 2019
The normative document number and its status (order, resolution, if applicable).	Mandatory for execution.
Legal status of recommendations: mandatory or advisory (What additional documents govern the need for recommendations).	Mandatory use of the document at the level of the healthcare facility.
Frequency of the document revision (Is it defined? What documents regulate this?).	The frequency of revision of the document is based on the frequency of the release of new WHO Guidelines. For the first time, the National Clinical Protocol for the Treatment of HIV Infection in the RT was developed in 2005, then it was revised in 2010, 2014, and 2019.
Level of evidence (description of the applicable system).	Based on the WHO Guidelines.
Members of the editorial board (Are representatives of NGOs/patient organizations included?).	The editorial team includes only specialists of various profiles (infectious disease specialists, TB, infectious disease clinicians) of the healthcare system. Representatives of public organizations are not included in the editorial staff of the revision of the Protocol.
List and a brief description of documents that additionally regulate the use of ARVs in the country, including the following documents, but not limited to: · Laws governing the nature of supplying the ARVs (free of charge/paid, by prepaid medical care plan or at the expense of a special national program, etc.); · Lists of vital and essential medicines; · Lists of medicines to be procured at the expense of different budgets; · Treatment standards, etc.	The Code of Health Care of the Republic of Tajikistan dated May 30, 2017, No. 1413, Chapter 24. Article 163: Rights of persons with HIV/AIDS "Free receipt of all types of qualified and specialized medical care, including medication, in public healthcare organizations." In the document "List of Essential Medicines", which is reviewed and approved annually by the Ministry of Health and Social Protection of the Population of the Republic of Tajikistan, includes all ARV drugs that are used in ART regimens. ARV drugs are not purchased from budget funds. "Guidelines on the diagnosis, monitoring and treatment of HIV infection in Tajikistan", page 28: "All HIV-infected persons (adults, adolescents, children under 15, pregnant women, patients with co-infection) are prescribed ART regardless of CD4 cells."

Page and quote from national protocols	Comment	Link to relevant WHO recommendation, page, document, quote
Part 2. Diagnostic recommendations		
Retesting before inclusion in care and treatment programs	**Document 1, page 9. Testing for HIV, pre- and post-test counseling. Confirming results:** "Retesting for HIV is recommended before starting ART for all confirmed HIV-positive individuals."	**The 2016 WHO Guidelines, page 19.** "WHO reminds national program implementers to retest all people newly diagnosed with HIV." Information note by the WHO from 22 October 2014: "Retest all HIV-positive, using the second specimen and involving the second laboratory technician with the same method and the testing algorithm, before the treatment and/or initiation of ART, regardless of ART initiation based on the CD4 count. Retesting people on ART is not recommended, as there are potential risks of incorrect diagnosis, particularly for in vitro diagnostics (IVDs) that use oral fluid specimens."
Pre-test and post-test advising services.	**Document 4, Chapter 5. Conditions for medical examination:** "Each medical examination for the detection of human immunodeficiency virus, regardless of its type, must be accompanied by pre-test and post-test psychosocial counseling."	**The 2016 WHO Guidelines:** "Counselling interventions were identified in eight included studies (seven cohort studies and one individual randomized controlled trial). Specific interventions included one-on-one post-test counselling, group counselling and counselling delivered by trained community members." **Page 245. Other approaches:** "WHO recommends that all HIV testing services should adhere to the five C's – consent, confidentiality, counselling, correct test results and connection (linkage to prevention, treatment and care services)... Taken together, the new recommendations and good practices outline a comprehensive set of interventions with demonstrated benefit to improve linkage from testing to care and ART initiation." **Page 247. Good practices for linkage from HIV testing services:** "Intensified post-test counselling by community health workers."
Testing by non-professional healthcare workers using express diagnostic methods.	**Order of the MHSPPRT, dated September 30, 2015, No. 832 "On permission to conduct HIV testing among KGP based on public organizations."** To improve the coverage of HIV testing among key populations, it is allowed to conduct rapid testing at NGOs that work in the field of HIV/AIDS prevention.	**The 2016 WHO Guidelines:** "New innovative approaches to HIV testing are being implemented, including home testing, community-based testing and self-testing." **Page 25. Task-sharing.** Recommendation: "Lay providers who are trained and supervised can independently conduct safe and effective HIV testing using rapid diagnostic tests (RDTs) (strong recommendation, moderate-quality evidence)." **Page 27. Community-based HIV testing services,** Concentrated HIV epidemic: WHO recommends community-based HIV testing services, with linkage to prevention, treatment and care, in addition to PITC for key populations (strong recommendation, low-quality evidence)."
Testing initiated by a healthcare worker.	**Document 4, page 6. Voluntary Medical Examination:** "Healthcare workers should recommend that individuals from the special populations with an increased risk of contracting the human immunodeficiency virus should undergo regular medical examinations for early detection of HIV infection, counseling, and timely treatment of infections."	

Diagnosis of HIV infection in children and infants, in particular, the sensitivity and specificity of tests.	According to sensitivity and specificity, the guideline is stated at the beginning of the document as a whole: Absolute (100%) sensitivity is the goal of any functioning system of HIV laboratory diagnostic. Specificity plays an equally important role and it is necessary that it also reaches 100%. And since no test system has 100 percent sensitivity and 100 percent specificity, the most sensitive tests should be used during the initial examination, and the most specific ones at the confirmation stage. **Testing Guide. Algorithm of HIV testing in RT, page 3.** Diagnosis of HIV infection in children born to HIV-infected mothers. In children under the age of 18 months, HIV infection is tested by PCR, the most highly sensitive method for detecting the genetic material of the virus in the cell. Biomaterial for research is venous whole blood or a dry drop of blood on filter paper. **31. Stages of the HIV diagnosis algorithm in children under 18 months of age (Regimen 4):** a) Diagnosis of HIV infection in an infant is carried out by PCR for HIV DNA at the age of 48 hours after birth; the material for the study of PCR DNA is FOB and/or whole blood. b) A positive PCR result is the basis for a diagnosis of HIV infection and an indication of the need to start ART. Regardless of the outcome, the second test should be repeated at 4-6 weeks of age. c) If a positive result is obtained at the age of 4-6 weeks, HIV infection is diagnosed, and the started ART is prescribed or continues. If the results of previous PCR studies are positive at the age of 3-4 months of life, the viral load (VL) is determined by RNA PCR, and ART is continued. d) When retesting (T1+) after 4-6 weeks, which gave a negative result (T2-), it is necessary to repeat the analysis by the same method on a new sample. e) If the PCR result is negative, the child remains in the observation group until the age of 18 months; an ELISA test is carried out to determine antibodies/ antigens to HIV. If clinical signs of HIV infection appear before the age of 18 months, PCR testing should be performed. If during the study at the age of 18 months by the ELISA method, no antibodies/ antigens to HIV infection were detected in a child, then the result is interpreted as negative and further observation is carried out as a healthy child. f) If the child is breastfed by an HIV-infected mother and at 18 months there are no antibodies/antigens to HIV infection in its blood, the study must be repeated 6 weeks after the cessation of breastfeeding (if before this term the child has clinical signs indicating HIV infection, the study should be conducted earlier).	**Consolidated Guidelines for HIV Testing Services 2015** For infants and children under 18 months, HIV infection can be diagnosed only by virological testing; maternal HIV antibodies remain in the infant's bloodstream until 18 months of age, making test results from serological assays ambiguous. Virological testing using nucleic acid testing (NAT) technologies can be conducted using dried blood spot (DBS) specimens, which are collected at local sites and sent to centralized laboratories for testing. While early testing is increasing, there are ongoing challenges of access, such as prompt return of test results and initiation of early ART among infants who test HIV-positive. Several approaches can increase infant testing. Scaling up early infant diagnosis (EID) through task-sharing with lay providers is one promising approach. Development, now underway, of virological assays for use at the point of care, is expected to greatly improve access to early diagnosis and treatment. HIV testing at the time of birth may improve linkage to treatment and reduce loss to follow-up; however, it is likely be an effective public health strategy only in settings with a high proportion of deliveries taking place in facilities. In any case, this approach would miss infant infections that take place during breastfeeding. For children 18 months of age and older (who were not breastfed or who have stopped breastfeeding at least six weeks earlier), standard HIV serological assays such as RDTs and EIAs can reliably determine HIV status. A negative serological test result for an infant does not completely exclude HIV exposure and infection, particularly when certain RDTs are used to test infants between four and 18 months of age, due to imperfect sensitivity during seroconversion for infection acquired postpartum through breastfeeding. During this time virological tests may be used to determine HIV infection.

Testing in special groups (adolescents, pregnant women, couples, and partners).	The testing guide used in the country does not have separate algorithms for pregnant women, adolescents, couples, and partners. All pregnant women who are registered for pregnancy at the PHC/ONF level are tested for HIV infection for up to 12 weeks of gestational development of the fetus or when the woman first visits the PHC/ONF. If for some reason a woman has not been tested for HIV at the ONF, then she is tested at the maternity hospital. All pregnant women are tested once, but retesting is recommended for all women with a high risk of infection (migrant husband, PWID husband, if the pregnant woman herself is a sex worker, etc.).	
Diagnostic algorithms.	**Testing Guide. Algorithm for HIV testing in the Republic of Tajikistan.** a) If a negative test result (T1-) is obtained, the specimen is recognized as not containing HIV serological markers. Further research is discontinued. The result is given to the patient. b) Upon receipt of a primary positive result (T1+), another study is carried out using a diagnostic test system of another manufacturer (T2) or using another research method: a study of a new specimen, if T1 is RT and a study of the same serum sample if T1 – ELISA. • If during the second analysis (T2) of the specimen a negative result was obtained (T1+; T2-), then it is necessary to repeat the first and second studies using the same specimen and the same tests (T1 and T2) to exclude laboratory errors. • A specimen that, when re-tested, gave two negative results (T1-; T2-), is recognized as HIV negative, further studies are stopped. The results are issued to the patient. c) If retesting gives a positive result in one test and negative in another (T1+; T2- or T1+; T2-; T3+), the patient must be retested after 14 days using a new blood/serum specimen. To resolve situations with conflicting test results, this algorithm provides for repeated testing after a specified time (at least 14 days), which is necessary to increase the concentration of antibodies/antigens in the blood to a detectable level or disappear the factors causing a non-specific reaction. d) A specimen that showed positive results in the first and second tests (T1+; T2+) must be sent to the laboratories of the regional center for the prevention and control of AIDS (RC AIDS), where the specimen is tested in the third test system (T3) to finally confirm the analysis. A blood specimen, confirmed for HIV infection, is sent to the State Institution "RC AIDS" for re-approval, registration, and storage. e) Before sending a positive specimen to the RC AIDS laboratory, the employees of the district laboratories of the AIDS centers must fill out an application, indicating all the data on the specimen and test results, enter all the data regarding the sent specimen into the electronic database of the tracking system. f) If a positive result is obtained after the third test (T1+; T2+; T3+) in the RC AIDS laboratory, HIV-positive status is registered and the patient must be monitored in the health care system. g) If a negative result is obtained after the third study (T1+; T2+; T3-), the specimen is registered as an inconclusive test for HIV infection. It is necessary to repeat blood sampling after 14 days and test it according to the above algorithm.	**Consolidated Guidelines for HIV Testing Services, July 2015. Page 120:** All specimens are first tested with one assay (A1), and specimens that are non-reactive (A1−) are considered HIV-negative and reported as such. A1 should be the most sensitive assay available, taking into account diagnostic sensitivity, seroconversion sensitivity, and analytical sensitivity. Any specimens that are reactive on the first assay (A1+) should be retested (tested again) using a separate and distinct second assay (A2) comprising a different antigen preparation to avoid false cross-reactivity with A1. For specimens that are reactive both on the first-line assay and the second-line assay (A1+; A2+), HIV status should be reported as HIV-positive. All individuals that are diagnosed HIV-positive should be retested prior to starting ART to verify their HIV-positive status (see section 3.4). Specimens that are reactive on the first-line assay but non-reactive on the second-line assay (A1+; A2−) should be repeated using the same specimen with the same two essays. When the test uses finger-stick whole blood, a new specimen will have to be taken and the same two assays repeated. Following repeated testing, if the results remain discrepant (A1+; A2−), the specimen should be retested (tested again) using a separate and distinct third-line assay (A3). · If the third assay is reactive (A1+; A2−; A3+), an HIV-inconclusive status is reported, and the client should be asked to return in 14 days for retesting. · If the third-line assay is non-reactive (A1+; A2−; A3−), the HIV status is reported as HIV-negative. If the first-line assay (A1) is a fourth-generation assay, however, the test result A1+; A2−; A3− should be reported as HIV-inconclusive, and the client should be asked to return for retesting in 14 days.

Part 3. ARV drugs for HIV prevention		
Pre-exposure prophylaxis of HIV infection.	The first steps have been taken to develop normative documents that disclose PrEP. **"Guidelines for the diagnosis, monitoring and treatment of HIV infection in Tajikistan", page 82.** Pre-exposure prophylaxis: "For people at high risk of HIV infection, PrEP is a new and important method of preventing the spread of HIV. Recommendations on PrEP should be provided by physicians from the Centers for the Prevention and Control of AIDS. Further observation of the patients on PrEP can be monitored at their place of residence (primary care facility).	**The 2016 WHO Guidelines, page 23:** "In prevention, clinical trial results have strongly confirmed the efficacy of the ARV drug tenofovir disoproxil fumarate alone or in combination with emtricitabine for use as pre-exposure prophylaxis (PrEP) to prevent HIV acquisition in a wide variety of settings and populations."
Algorithm and regimens of post-exposure prophylaxis for different population groups, including PMTCT.	**Order of the MHSPPRT, dated September 30, 2009, No. 597 "Manual for the prevention of HIV transmission at the workplace" and also in the document "Guidelines for the diagnosis, monitoring and treatment of HIV infection in Tajikistan," page 26:** "Regimens for PEP should consist of 2 drugs, or 3-component therapy can be used: of the NRTI group (preferred is TDF/FTC), of PI groups (preference is LPV/r or ATV/r). Preferred PEP regimens for children under 15 years: AZT/3TC. Alternative - ABC/3TC or TDF/FTC. The duration of administration is 28 days." **Testing: Order of the MHSPPRT, No. 597, dated September 30, 2009, page 15:** Follow-up of the patient: "HIV testing is done immediately after exposure, 6 weeks, 12 weeks, and 6 months, even if no PEP was given."	**The 2016 WHO Guidelines, PEP. Page 62:** "A regimen for post-exposure prophylaxis for HIV with two ARV drugs is effective, but three drugs are preferred (conditional recommendation, very low-quality evidence). Post-exposure prophylaxis ARV regimens for adults and adolescents: • TDF + 3TC (or FTC) is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis for adults and adolescents (strong recommendation, low-quality evidence). • LPV/r or ATV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for adults and adolescents (conditional recommendation, very low-quality evidence). Where available, RAL, DRV/r, or EFV can be considered as alternative options. Post-exposure prophylaxis ARV regimens for children ≤10 years: • AZT + 3TC is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis for children aged 10 years and younger. ABC + 3TC or TDF + 3TC (or FTC) can be considered as alternative regimens (strong recommendation, low-quality evidence). • LPV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for children younger than 10 years (conditional recommendation, very low-quality evidence). An age-appropriate alternative regimen can be identified among ATV/r, RAL, DRV, EFV, and NVP."

Part 4. Antiretroviral therapy regimens		
When ART should be started, including recommendations for specific groups of patients (for whom urgent indication is recommended).	**Document 1, page 25. Important work before ART initiation:** "Patients in the late stage should be closely monitored and their conditions should be regularly checked and controlled. The following symptoms indicate progressive stages: 1. For adults, adolescents, and children over 5 years of age, the clinical stage is 3 or 4 or CD4 less than 200 cells/mm3. All children under 5 years of age, regardless of clinical symptoms and CD4 count. 2. All adults and adolescents with a respiratory rate of more than 30 times per minute; pulse more than 120 times per minute; a patient who is in a difficult situation and cannot move without assistance. 3. Children with severe concomitant diseases and signs of pathological symptoms; "Persons in stable condition (in the first and second clinical stages) should be advised to start antiretroviral therapy, viral load, and CD4 test on the first day of detection, regardless of CD4 count." **Page 28.** "Important: Antiretroviral treatment should be initiated for all adolescents and adults living with HIV, pregnant or breastfeeding women, children under the age of 15, regardless of the clinical stage of the disease and regardless of CD4 count. Pregnant women should receive treatment regardless of the gestational age. In addition, ART should be started in all people living with HIV, regardless of CD4 count."	**The 2016 WHO Guidelines, page 74.** **4.3 When to start ART:** "ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count (strong recommendation, moderate-quality evidence). As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤350 cells/mm3 (strong recommendation, moderate-quality evidence)."
Choice of first-line drugs, incl.	**Preferred first-line ART regimens for adults and adolescents :** TDF + 3TC (or FTC) + DTG. **For children 3-15 years old:** ABC + 3TC + RAL or EFV or NVP; AZT + 3TC + RAL or EFV or NVP; TDF + FTC + RAL or EFV or NVP. **For newborns to 3 years (36 months):** ABC or AZT + 3TC + LPV/r (or NVP,) if a RAL preparation is available, then it must be used. **Alternative first-line ART regimens for adults and adolescents :** TDF + 3TC (or FTC) + EFV.	
Preferences for fixed-dose combination (FDCs) drugs	**Document 1, page 29.** Dosage and ART regimens for use must be in the FDC.	**The 2016 WHO Guidelines, page 105:** "Fixed-dose combinations and once-daily regimens are preferred for antiretroviral therapy (strong recommendation, moderate-quality evidence)."
Refusal to use stavudine	Since 2010, there is no stavudine in the protocols.	**The 2016 WHO Guidelines, page 290:** 6.13.3 Special considerations for adult and adolescent ART regimens: "Stavudine (d4T): in light of the cumulative mitochondrial toxicity of d4T, it should no longer be procured, and people currently receiving d4T-based regimens should transition to a TDF-based regimen."

Use of DTG and EFV400 in accordance with the updated recommendations (2018, 2019)	**Document 1, page 29.** "Important! The composition of the drug TDF + 3TC (or FTC) + DTG is recommended as the preferred form of ARV regimens in combination with defined dosage." **Document 1, page 68.** "Consider the possibility to use low dose EFV (400 mg per day).	**The 2016 WHO Guidelines, page 289:** 6.13.3 Special considerations for adult and adolescent ART regimens: "DTG and EFV 400 mg/day are recommended as alternative first-line agents." **The 2019 WHO Guidelines, page 5:** First-line ART regimens: "DTG in combination with an optimized NRTI backbone may be recommended as a preferred second-line regimen for people living with HIV for whom non-DTG-based regimens are failing. · Adults and adolescents (conditional recommendation, moderate-certainty evidence) · Children with approved DTG dosing (conditional recommendation, low-certainty evidence)" Efavirenz at a low dose (EFV 400 mg) in combination with an NRTI backbone is recommended as the alternative first-line regimen for adults and adolescents living with HIV initiating ART (strong recommendation, moderate certainty evidence)
Recommendations for use of dolutegravir in women of childbearing age and pregnant women	**Document 4, page 29.** "Important! DTG is not recommended for pregnant women. Women who received ART regimens with DTG should switch to another ART regimen during pregnancy (if RAL is available, if not, then use EFV) and then return to backbone one after childbirth.	
First-line ART for special patient groups.	**Document 1, page 29:** "If there are any restrictions to prescribe preferred or alternative ART regimens, it is necessary to prescribe the following ART regimens in such special cases: AZT + 3TC + DTG; AZT + 3TC + EFV.	**The 2016 WHO Guidelines, page 147.** Table 4.2 First-line ART regimen for adults: "Special circumstances: Regimens containing ABC and boosted PIs. Special circumstances may include situations where preferred or alternative regimens may not be available or suitable because of significant toxicities, anticipated drug–drug interactions, drug procurement and supply management issues, or for other reasons." **The 2019 WHO Guidelines, table number 1.** Preferred first-line ART regimens for special circumstances. **Adults:** TDF + 3TC (or FTC) + EFV 600 mg, AZT + 3TC + EFV 600 mg, TDF + 3TC (or FTC) + PI/r TDF + 3TC (or FTC) + RAL, TAF + 3TC (or FTC) + DTG, ABC + 3TC + DTG. **Children:** ABC + 3TC + EFV (or NVP), AZT + 3TC + EFV (or NVP), AZT + 3TC + LPV/r (or RAL). **Neonates:** AZT + 3TC + LPV/r.
Recommendations for breastfeeding of babies.	**Document 4, page 31.** ART: "All newborns born to HIV positive mothers should be breastfed. In the Republic of Tajikistan, all children born to HIV-positive mothers are encouraged to receive infant formula free of charge for 18 months after birth, as required by the Code of Health Care." **Document 2 (Code of Health Care of the Republic of Tajikistan).** Article 163. Rights of PLHIV. Part 1, paragraph 7: "Parents or legal representatives of children born to mothers infected with the human immunodeficiency virus receive breast milk substitutes from the moment of their birth until the time they are finally diagnosed with the human immunodeficiency virus, to further reduce the risk of infection with the human immunodeficiency virus."	**The 2016 WHO Guidelines:** "The risk of HIV transmission persists as long as breastfeeding continues." **The 2016 WHO Guidelines, page 30:** "PITC for women should be considered a routine component of the package of care in all antenatal, childbirth, postpartum and pediatric care settings. In such settings, where breastfeeding is the norm, lactating mothers who are HIV negative should be retested periodically throughout the period of breastfeeding." **The 2016 WHO Guidelines, page 35:** "National or subnational health authorities should decide whether health services will principally counsel and support mothers known to be HIV infected to either breastfeed and receive ARV interventions or avoid all breastfeeding."

Monitoring before and after starting ART.	**Document 4, page 32.** **ART monitoring:** "Continuous viral load monitoring should be performed at intervals of 6 months and 12 months after treatment, and then every 12 months if viral loads are less than 1000 copies/ml. CD4 monitoring may be discontinued, if continuous monitoring of viral load is possible, the client's condition is stable on ART, and viral load is undetectable." **Document 4, page 33:** "Important! Individuals, if they are on antiretroviral therapy with viral loads of less than 1000 copies/ml and CD4 counts of more than 350 cells/mm3, should be screened once or twice a year. In case of effective treatment, patients can receive ARVs for a period of 6 months or up to 1 year. "	**The 2016 WHO Guidelines, p. 128:** "HIV viral load (at 6 months and 12 months after initiating ART and every 12 months thereafter) CD4 cell count every 6 months until patients are stable on ART." **Page 129:** "Routine viral load monitoring can be carried out at 6 months, at 12 months and then every 12 months thereafter if the patient is stable on ART to synchronize with routine monitoring and evaluation reporting (conditional recommendation, very low-quality evidence). In settings where routine viral load monitoring is available, CD4 cell count monitoring can be stopped in individuals who are stable on ART and virally suppressed (conditional recommendation, low-quality evidence). "
Recommendations for switching to second-line ART regimens, including special patient groups, and a preferred alternative regimen.	**Document 1, page 35.** **Treatment failure:** "If 6 months after starting first-line ART, viral load is> 1000 copies/ml, this can be considered as a possibility of treatment failure. Repeat viral load for 3 months to confirm the possible failure of virologic treatment or not confirm it. In case of high viral load (>1000 copies/ml), the treatment plan must be changed. If in doubt, another viral load test is required before changing the plan." **Page 38:** 1. Preferred second-line ART regimen: 2NRTIs (AZT + 3TC) + 1 INSTI (DTG) or TLD, or PI (ATV/r or LPV/r). 2. Alternative second-line ART regimen: 2 NRTIs + DRV/r. **Page 39:** Second-line ART regimens for children under 15 years. Up to 3 years: switch from LPV/r to RAL. Children from 3 to 15 years old: switch from LPV/r to EFV or RAL. "Once NNRTI-based first-line treatment failure has been determined, the need to select 3 drugs from the PI group with ritonavir-boosted LPV/r or ATV/r will be better." "If, after the failure of a first-line ART regimen based on ABC or TDF + 3TC (or FTC), the preferred second-line regimen should be selected based on AZT + 3TC."	**The 2016 WHO Guidelines, page 14:** Viral failure refers to the inability to achieve or maintain viral suppression below a certain threshold. Viral failure is defined by a persistently detectable viral load exceeding 1000 copies/mL (two consecutive viral load measurements within a 3-month interval with adherence support between measurements) after at least 6 months of using ART. **The 2016 WHO Guidelines, page 5:** **Note 1. Recommendations for first- and second-line ART regimen.** The updated evidence reviews assessed the efficacy and safety of DTG in combination with an optimized NRTI backbone for people for whom a non-DTG-based first-line regimen has failed. · Adults and adolescents (conditional recommendation, medium confidence) · Children on DTG Registered Dose (Conditional Recommendation, Low Confidence). **Preferred ART regimens for adults:** AZT + 3TC + ATV/r (or LPV/r); AZT + 3TC + DTG; TDF + 3TC (or FTC) + DTG. **Preferred ART regimens for children and infants:** AZT + 3TC + LPV/r (or ATV/r); AZT (or ABC) + 3TC + DTG. **Alternative ART regimens for adults:** AZT + 3TC + DRV/r (or NVP); AZT + 3TC + ATV/r (or LPV/r or DRV/r); TDF + 3TC (or FTC) + ATV/r (or LPV/r or DRV/r). **Alternative ART regimens for children and infants:** AZT + 3TC + DRV/r; AZT (or ABC) + 3TC + RAL; AZT (or ABC) + 3TC + LPV/r (or ATV/r); ABC + 3TC + LPV/r (or ATV/r) or DRV/r.

Recommendations for the third-line ARVs.	**Document 1, page 40.** **Failure of ART:** "In case of failure of second-line ART, it is necessary to consult with specialists of the republican level." "Third-line ART should include new drugs with minimal risk of compatibility with previous drugs, such as INSTI, second-generation NNRTIs, and PIs." "Important! Where possible, conduct a drug resistance test before changing a treatment regimen."	**The 2016 WHO Guidelines, page 157:** **4.8.3 Third-line ART.** · National programmes should develop policies for third-line ART (conditional recommendation, low-quality evidence). · Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as INSTIs and second-generation NNRTIs and PIs (conditional recommendation, low-quality evidence). · Patients on a failing second-line regimen with no new ARV drug options should continue with a tolerated regimen (conditional recommendation, very low-quality evidence). **Page 161.** Table 4.19. Summary of sequencing options for first-, second- and third-line ART regimens in adults, adolescents, pregnant women and children **Adults and adolescents (> 10 years), pregnant and breastfeeding women:** DRV/r + DTG (or RAL) ± 1–2 NRTI. **Children (0-10 years):** RAL (or DTG) + 2 NRTI; DRV/r + 2 NRTIs; DRV/r + RAL (or DTG) ± 1–2 NRTI.
Barriers to accessing key drugs recommended by WHO, when they are available (e.g., no registration, no inclusion in the list of vital and essential medicines or procurement lists, high price, etc.)	No	N/A
Part 5. Prevention and treatment of concomitant infections and diseases		
Recommendations for the prevention and treatment of co-infections, primarily (but not limited to): · HIV/HCV · HIV/HBV	**Document 1, page 60.** **Opportunistic infections in HIV:** "One of the main problems is that in most cases HIV-infected people have HIV/HCV/HBV co-infection. In this regard, an integrated approach is very important, which is more important as: 1. Prevention; 2. Test for hepatitis B and C; 3. Vaccination against hepatitis B; 4. Treatment and care for clients with co-infections: HIV/HBV and HIV/HCV. If testing of PLHIV shows a negative result for HBV, then it is recommended to vaccinate against hepatitis B." "Screening for HCV (test for antibodies to hepatitis C virus) is recommended for all HIV-infected once a year." **Page 61:** "Treatment of viral hepatitis B and C is carried out in accordance with existing treatment protocols."	**The 2016 WHO Guidelines, page 209:** In 2011, in the Consolidated Guidelines for the Use of Antiretroviral Drugs, WHO recommended that ART be prescribed to all people with HIV/HBV co-infection regardless of CD4 cell count, and with signs of severe chronic liver disease. This recommendation has now been superseded by a new 2015 recommendation which specifies that treatment should be provided to all people living with HIV regardless of CD4 cell count. "Recommended NRTI drugs for ART (TDF (TDF) and 3TC (3TC) or FTC (FTC)) are active for HBV." "Hepatitis C virus (HCV)-related liver disease progresses more rapidly in people coinfected with HIV. Treatment of HCV is therefore a priority for people with HIV/HCV coinfection."

HIV/TB	**Page 41:** "Important! All people living with HIV should be screened for tuberculosis. If the afore-mentioned signs (4 symptoms) are present, then a chest R-graph and laboratory test to rule out or confirm TB is required. If a person living with HIV is on ART, his/her VL is undetectable, CD4 count is high, he/she has received TB prophylaxis and has no clinical signs (fever, cough, night tremors, and weight loss), it is not necessary to take R-chest graph." "Screening for TB provides a basis for PLHIV who need to be prescribed CPI. Patients with active tuberculosis are not required to test for tuberculosis during treatment. "	**The 2016 WHO Guidelines:** "ART should be started in all TB patients living with HIV, regardless of CD4 cell count (strong recommendation, high-quality evidence). TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment (strong recommendation, high-quality evidence). HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm3) should receive ART within the first two weeks of initiating TB treatment.
Prevention and treatment of relevant non-communicable diseases: Cardiovascular diseases	**Document 1, pages 58, and 59.** "It is recommended to assess and monitor the risk of CVD among HIV-infected people based on standard clinical protocols for the whole population." It is recommended to conduct electrocardiography, lipid metabolism tests, blood sugar, blood pressure indicators when detected, before ART, and then once a year."	
Depression	**Page 59:** "Assessment and monitoring of depression should be included in the package of activities for PLHIV and available to all HIV-infected people." "If PLHIV needs help, it is necessary to organize a consultation with a psychologist or a medical psychologist. If the centers do not have the psychologist, then family doctors or infectious disease specialists can contact the psychologist by phone and the Internet to receive advice. Treatment or counseling can be done individually or in groups. In severe cases, drug therapy can be conducted."	**The 2016 WHO Guidelines, page 219:** Part 5.3.2 Assessment and management of depression in people living with HIV. Recommendation "Assessment and management of depression should be included in the package of HIV care services for all individuals living with HIV (conditional recommendation, very low-quality evidence)." **Page 220:** "Though depression is more common among people with HIV compared to the general population, there is less consistent and limited evidence to show that management of depression improves HIV treatment outcomes. However, management of depression improves mental health and general well-being in people with HIV." "Screening for depression may support adherence to ART, retention in care and viral load suppression and improve the quality of life. If implemented, depression should be managed according to national standards or mhGAP."
Diseases of the central nervous system	No information.	
Kidney disease	The clinical guidelines specify the control of renal function in patients on ART including TDF in ART regimens.	
Substance use	The country uses a comprehensive package of services of nine types of prevention, treatment, and care measures for HIV-positive PWID: · Needle and syringe programs; · Opioid substitution therapy; · HIV counseling and testing; · ART; · Prevention and treatment of sexually transmitted infections; · Condom support programs; · Targeted outreach activities to promote behavior change; · Prevention and treatment of viral hepatitis; · Prevention, diagnosis, and treatment of TB."	**The 2016 WHO Guidelines, page 221:** Part 5.3.3 Drug use and drug use disorders. "People living with HIV who use drugs may experience a range of disorders related to drug use, including drug dependence, intoxication, withdrawal and overdose. Injecting drug use is associated with a range of diseases and infections, including viral hepatitis, TB, septicaemia and bacterial endocarditis, in addition to HIV." "WHO, the United Nations Office on Drugs and Crime (UNODC) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) recommend a comprehensive package of nine interventions for HIV prevention, treatment and care for people who inject drugs; these are needle and syringe programmes, OST, HIV testing and counselling, ART, preventing and treating STIs, condom programmes, targeted behaviour change communication, preventing and treating viral hepatitis and preventing, diagnosing and treating TB."

Part 6. Health service provision

The provision of health services, including but not limited to: • Recommendations for the decentralization of services. • Recommendations for redistribution and delegation of services. • Recommendations for integration of services.	Order of the MHSPPRT, dated April 17, 2019, No. 252 "On the organization and implementation of joint services, including medical and social (integration) for the prevention, diagnosis, and treatment of HIV infection among adults and adolescents at the level of primary health care (PHC)." Approve all reporting forms (annexes 2, 3, 4, and 5) (Page 1 of the order). All heads of regional health departments and district health departments should implement this order at the local level. And all PHC managers should also introduce these services at the primary level. By order of the institutions, to approve one family doctor as responsible for HIV to inform the population about HIV infection and one infectious disease specialist to monitor patients with HIV infection and prescribe treatment, as well as monitoring of treatment (Annex 1 of the order). Organize an office providing all the equipment and storage of ARV drugs and drugs for the treatment and prevention of OI. Provide training for specialists involved in the treatment and monitoring of HIV-infected patients. Republican, city, and regional AIDS Centers should directly conduct mentoring visits, re-train and assist specialists at the workplace.	**The 2016 WHO Guidelines, page 246:** Good practices for linkage from HIV testing services: • "Comprehensive home-based HIV testing, which includes offering home assessment and home-based ART initiation • Integrated services, where HIV testing, HIV prevention, treatment and care, TB and sexually transmitted infection (STI) screening and other relevant services are provided together at a single facility or site • Providing on-site or immediate testing for CD4 cell count with same-day results • Providing assistance with transport, such as transportation vouchers, if the ART site is far from the HIV testing service site • Decentralized ART provision and community-based distribution of ART • Support and involvement of trained lay providers who are peers and act as peer navigators, expert patients/clients and community outreach workers to provide support, and identify and reach people lost to follow-up • Intensified post-test counselling by community health workers • Using communication technologies, such as mobile phones and text messaging, which may help with disclosure, adherence and retention, particularly for adolescents and young people • Providing brief strengths-based case management, which emphasizes people's self-determination and strengths, is client-led and focuses on future outcomes, helps clients set and accomplish goals, establishes good working relationships among the client, the health worker and other sources of support in the community and provides services outside of office settings • Promoting partner testing may increase rates of HIV testing and linkage to care, as may approaches that encourage male involvement in prevention of mother-to-child transmission (PMTCT) settings • Intimate partner notification by the provider, with permission, is feasible in some settings; it identifies more HIV-positive people and promotes their early referral to care."

Uzbekistan

Part 1. Basic information	
Name of the current version of the document and the link to it.	"On implementing national clinical protocols for HIV infection into practice", Annex 1 to Order of the MoH of RU, No. 277, dated April 30, 2018.
Year of the current version.	2018
The normative document number and its status (order, resolution, if applicable).	1. Order of the MoH of RU No. 277, dated April 30, 2018 "On implementing national clinical protocols for HIV infection into practice", volumes 1 and 2. 2. Annex to Order No. 200 of the MoH of RU, dated June 12, 2014 "On the introduction of rapid testing among key populations." 3. Order of the MoH of RU, No. 336, dated May 24, 2018, "On measures to prevent HIV infection in the Republic of Uzbekistan and further improve the management of health care."
Legal status of recommendations: mandatory or advisory (What additional documents govern the need for recommendations).	The legal status of the recommendations: Mandatory for execution. 1. Resolution of the President of the Republic of Uzbekistan "On measures to further improve the system of countering the spread of the disease caused by the human immunodeficiency virus in the Republic of Uzbekistan," No. 3493, dated January 25, 2018, paragraph 5 of the state program. 2. Resolution of the President of the Republic of Uzbekistan "On additional measures to counteract the spread of the disease caused by the human immunodeficiency virus, and the prevention of nosocomial infections," dated January 25, 2018, paragraph 10 of the state program.
Frequency of the document revision (Is it defined? What documents regulate this?).	The frequency of revision of the document is not regulated by any documents in the country.
Level of evidence (description of the applicable system).	
Members of the editorial board (Are representatives of NGOs/patient organizations included?).	The editorial staff included: 1. Decision-makers at the level of the Ministry of Health: Deputy Minister of Health, Chief Sanitary Doctor of the Republic of Uzbekistan, in charge of the AIDS service; Chief Epidemiologist of the Republic of Uzbekistan; Chief Infectious Disease Specialist of the Republic of Uzbekistan; Chief Pediatric Infectious Disease Specialist of the Republic of Uzbekistan; 2. Leading specialists: Republican AIDS Center and regional AIDS Centers; Institute of Obstetrics and Gynecology, Phthisiology and Pulmonology; 3. Lecturers of the Institute of Postgraduate Education: Tashkent Institute of Advanced Medical Education: Department of Infectious Diseases, Department "Problems of HIV Infection"; Department of Infectious and Children's Infectious Diseases at the Tashkent Medical Academy; teachers of the training center for the treatment, care and support of HIV-infected people. The editorial board did not include representatives of community/patient organizations.
List and a brief description of documents that additionally regulate the use of ARVs in the country, including the following documents, but not limited to: · Laws governing the nature of supplying the ARVs (free of charge/ paid, by prepaid medical care plan or at the expense of a special national program, etc.); · Lists of vital and essential medicines; · Lists of medicines to be procured at the expense of different budgets; · Treatment standards, etc.	**Law of the Republic of Uzbekistan "About counteraction to spread of the disease caused by human immunodeficiency virus (HIV infection)", 22.08.2013** **Chapter 3, Article 17:** "Provision of medical care to HIV-infected people": Free specific treatment for HIV-infected people is prescribed based on the conclusion of a medical commission, depending on the stage of the disease in AIDS centers, in departments of healthcare facilities for HIV-infected people. **Chapter 3, Article 20:** Free specific treatment is provided for people living with HIV. **Chapter 5, Article 22:** Financing of activities to counter the spread of HIV infection is conducted at the expense of the State budget of the Republic of Uzbekistan, as well as other sources not prohibited by law. **Law of the Republic of Uzbekistan "On Pharmaceuticals and Pharmaceutical Activities," Article 24:** The import of orphan medicines can be conducted without state registration.

	Resolution of the President RP-3493 of the Republic of Uzbekistan "On measures to further improve the system of counteracting the spread of the disease caused by the human immunodeficiency virus in the Republic of Uzbekistan," No. 3493, dated January 25, 2018, paragraphs of the state program**:** **Paragraph 4:** It is envisaged to introduce into medical practice specific prophylaxis with antiretroviral drugs for HIV-negative persons in discordant couples. **Paragraph 5:** Step-by-step transition to a specific treatment (APT) of all identified HIV-infected people from the confirmation of the diagnosis and registration for follow-up monitoring (Stage 1: providing treatment to all HIV-infected persons under the age of 18 regardless of CD4 count; Stage 2: providing treatment for all HIV-infected persons under the age of 30 regardless of CD4 count; Stage 3: treatment of all HIV-infected persons regardless of CD4 count. **Paragraph 13:** It is foreseen for 2018 the need to allocate funds from the State budget for the provision of antiretroviral drugs and test systems to monitor the effectiveness of treatment of HIV-infected people.
	Resolution of the President of the Republic of Uzbekistan RP-3800 "On additional measures to counteract the spread of the disease caused by the human immunodeficiency virus and the prevention of nosocomial infections," dated January 25, 2018, Paragraph 10 of the state program**:** A comprehensive set of additional measures to increase the effectiveness of measures taken to counter the spread of HIV infection and the prevention of nosocomial infections was approved; the main directions were determined for further improvement and expansion of healthcare and social assistance provided to the population to prevent, diagnoses and treat HIV infection, a gradual increase in the size of budgetary allocations to the uninterrupted provision of healthcare and preventive institutions with antiretroviral drugs, as well as stable financing of measures to counter the spread of HIV infection in the republic for 2019-2022. **Paragraph 10:** There is a need to allocate funds from the State budget for the uninterrupted provision of antiretroviral drugs to prevent and treat HIV infection, cover low-income people living with HIV with antiretroviral therapy for 2019-2020.
	2016 Essential Medicines Formulary: The list of essential drugs includes 22 titles of ARV drugs that are recommended for use in HIV treatment.
	Order No. 230, dated July 5, 2014, "On standard operating procedures for managing the provision of antiretroviral drugs and diagnostics": A mechanism for the centralized procurement and provision of antiretroviral therapy was approved, and the heads of healthcare and preventive institutions and territorial AIDS centers hold responsible for coordinating measures to ensure the continuity of supplies of antiretroviral drugs, as well as monitoring the availability of the necessary supply of antiretroviral drugs in health facilities. A mechanism for predicting the need for ARV drugs and the regularity of reporting on ARV drug consumption are described.
	Order of the MoH of RUz, No. 249, dated June 06, 2016, "On the introduction of the third-line antiretroviral therapy in cases of the ineffectiveness of the second line": The order makes it possible to use the third-line therapy in cases of the ineffectiveness of the second-line therapy and recommends purchasing and using the following regimens for third-line therapy. A list of ARV drugs for the third-line therapy and the treatment regimens themselves are given.
	Order of the MoH of RUz, No. 316, dated June 4, 2019, "On approval of the list of orphan medicines for the treatment of rare diseases"**:** This order allows ARV drugs to be imported into the country through customs control and used without registration and certificate of conformity. This document contains all the names and forms of ARV drugs used in the country.
	Order of the MoH of RUz, No. 336, dated May 24, 2018 "On measures to prevent HIV infection in the Republic of Uzbekistan and further improve the management of medical care": The document promotes the interaction of the AIDS service with other healthcare services and also indicates the mechanism of their cooperation with other departments and organizations for the effective implementation of the National Action Plans approved by RP3493 and RP-3800, which contributes to ensuring universal access, monitoring of ARV therapy beginning from AIDS centers to primary health care (Infectious Disease Rooms at district level).

	Order of the MoH of RUz, No. 277, dated April 30, 2018, "On implementing national clinical protocols for HIV infection into practice": This order regulates the implementation of 14 national clinical protocols in healthcare facilities in all areas of medical services for HIV-infected persons, including ART, adapted based on WHO protocols and guidelines. **Protocol 2. Consolidated national clinical protocol "Use of ARV drugs for the treatment and prevention of HIV infection"** regulates the priority of initiating ART for patients depending on the CD4 count, the preferred ARV regimens, their side effects, possible ARV drug substitutions depending on the age and concomitant diseases. **Protocol 3. "Standard operating procedures on the mechanism for the provision of antiretroviral drugs and diagnostics"** describes the mechanism for predicting the number of patients on ART, drawing up an annual plan for the provision of ART, annual developing and approving the National Plan for the provision of ART, budgeting for the procurement of ARV drugs, distributing and delivering ARV drugs to the regions of the country and all patients. **Protocol 4. "Tuberculosis and HIV infection: management tactics for people with co-infection"** recommends using standard ARV treatment regimens in patients with TB/HIV co-infection, the combination of ARV drugs with anti-tuberculosis drugs, possible side effects of ARV drugs having tuberculous treatment. **Protocol 7. "Antiretroviral drugs for the prevention of HIV infection (PEP and PrEP)"** specifies ARV drug regimens doses and duration of their use recommended for the course of Postexposure Prophylaxis; the section on oral PrEP for HIV-negative partners describes the use of TDF and 3TC in combination, their duration of use, possible side effects, monitoring the effectiveness of prevention. **Protocol 8. "Viral hepatitis B and HIV infection: tactics of managing patients with co-infection"** outlines the management of patients with HBV/HIV co-infection, indicates antiretroviral drugs for the treatment of combined hepatitis B and HIV infection (3TC, ETV, TDF, FTS), gives recommendations on the initiating ART in patients with HBV/HIV co-infection, first-line and third-line ART regimens for patients with HBV/HIV co-infection. **Protocol 12. "Prevention of mother-to-child transmission of HIV"** describes the observation, examination, and initiation of ARV therapy for an HIV-infected woman during pregnancy; clinical scenarios and tactics during the pregnancy, childbirth and postpartum period with the use of ARV drugs, as well as the use of ARV drugs for newborn children born to HIV-infected mothers; dosages of syrup forms used for babies.
	Resolution of the Ministry of Internal Affairs of the RUz and the MoH of RUz, dated December 20, 2018, No. 82/59 "On approval of the Instructions on organizing provision of health care and antiretroviral therapy to HIV-infected persons held in pre-trial detention centers and correctional facilities of the Ministry of Internal Affairs of the Republic of Uzbekistan": An approved instruction describes the procedure for the provision of medical care and the provision of ART to HIV-infected persons held in pre-trial detention centers and penitentiary facilities of the Ministry of Internal Affairs of the Republic of Uzbekistan; the mechanism for the provision of ARV drugs to the system of the Main Directorate for the Execution of Sentences; forms of reporting of patients according to treatment regimens, ARV drugs, and their residues, which should be provided monthly to the MoH of RUz to monitor treatment.
Other significant information	**Analytical review of the legislation on human rights in the context of HIV/AIDS of the Republic of Uzbekistan:** A comprehensive strategy for the provision of ART is being implemented through the state nationwide network that consists of the Republican AIDS Center and 14 regional (Republican, regional and city (Tashkent)) AIDS Centers, and the system of the Main Directorate for the Execution of Sentences. Fourteen AIDS centers have access to laboratory tests to determine over time viral load (effectiveness of ART) of people living with HIV. In 2014, Uzbekistan began the provision of ART at the expense of the state budget, gradually increasing the share of state funds. **Order of the MoH of RUz, No. 277, dated April 30, 2018, "On the implementation of national clinical protocols for HIV infection into practice":** Foreign citizens have the right to receive ART only after official registration in AIDS centers.

Page and quote from national protocols	Comment	Link to relevant WHO recommendation, page, document, quote
Page 30. Antiretroviral therapy: Before starting ART, healthcare providers should have a detailed discussion of patients' willingness and readiness to initiate ART, about ARV treatment regimen, dosages, schedule of administration, possible benefits, possible side effects, and necessary follow-up, monitoring visits. If it is about the HIV-infected child, this conversation should take place directly with the person who cares for the child, and about the issues of the child's HIV status disclosure.	It complies with the 2016 WHO Guidelines.	**Page 72. Preparing people living with HIV for ART:** Before people start antiretroviral therapy (ART), healthcare providers should initiate a detailed discussion about the willingness and readiness of patients to initiate ART, the antiretroviral (ARV) drug regimen, dosage, scheduling, likely benefits, possible adverse effects and the required follow-up and monitoring visits. In the case of children with HIV, this conversation should directly involve the caregiver and include discussion about disclosing their HIV status.

	These 2016 and 2019 WHO Guidelines are absent in the national protocol, as the country has not yet adopted the recommendation: "Western blotting and linear immunoassay should not be used in HIV testing strategies/ algorithms". The diagnosis of HIV infection is made only based on 2 ELISA positive results and then a positive Western blot assay. Before starting ART, the patient does not have a rapid HIV test. Perhaps, for this reason, the number of people who know their HIV status is less than 70% according to the estimated number of PLHIV. The existing HIV diagnostic algorithm complicates not only the timely prescription of ART but also the provision of preventive services to people who are constantly at increased risk of infection.	**Page 72. Preparing people living with HIV for ART:** Retesting all people living with HIV before initiating ART is recommended to ensure a correct diagnosis of HIV infection. Initiation of ART should always consider nutritional status, any comorbidities and other medications being taken to assess for possible interactions, contraindications and dose adjustment.
Page 30. Antiretroviral therapy: The decision of whether to initiate or refuse ART is ultimately made by the person or their caregivers; if they decide not to start ART, they may be offered treatment again at subsequent visits. If the person faces mental health or drug abuse problems, or other potential barriers to starting ART or adherence to treatment, the client should be provided with the necessary support and re-assessed his/her willingness to initiate ART at regular intervals. Community and social group support can help the person be prepared and decide to start therapy.	It complies with the 2016 WHO Guidelines.	**Page 72: Preparing people living with HIV for ART:** The choice to accept or decline ART ultimately lies with the person or his or her caregiver, and if they choose to defer initiation, ART can be offered again at subsequent visits. If the person faces mental health or substance use issues or other potential barriers to ART initiation or adherence, appropriate support should be provided and readiness to initiate ART should be reassessed at regular intervals. Community and peer support can help a person to prepare and make the decision to start therapy.
Page 30. Antiretroviral therapy: Persons who initiate the treatment and their caregivers should be advised that the first ART regimen offers the best opportunity for effective virologic suppression, immunosuppression, and, therefore, clinical benefit and that for a successful ART outcome, all drugs must be taken how they are prescribed. It is important to know that possible delays in ART initiation can have negative consequences, in particular for people with TB or severely immunosuppressed people who are at high risk of death. The patient's attention should be drawn to the fact that many undesirable effects are temporary or can be controlled, and that often ARV drugs associated with undesirable effects can be replaced by others. While preparing to initiate treatment, it is important to assess the patient's need for psychosocial support to achieve optimal adherence to treatment. People on ART and caregivers should regularly be asked about their other medications, including herbal medicines and nutritional supplements. People starting ART should receive advice on safer sex, in particular the use of condoms, and on the need to avoid other risky activities, such as sharing injecting materials, to prevent HIV transmission to others.	It complies with the 2016 WHO Guidelines.	**Page 72. Preparing people living with HIV for ART:** People starting treatment and caregivers should be informed that the first ART regimen offers the best opportunity for effective viral suppression, immune recovery and consequently clinical benefit and that successful ART requires all medications to be taken as prescribed. It is important to acknowledge that there are situations where delays in starting ART can have negative consequences, particularly for people with tuberculosis (TB) or advanced immunosuppression, who are at high risk of death. People should be advised that many adverse effects are temporary or may be treated and that substitutions can often be made for the ARV drugs associated with adverse effects. In preparation for treatment initiation, it is important to assess the need for psychosocial support to optimize adherence. People receiving ART and caregivers should also be asked regularly about any other medications that are being taken, including herbal remedies and nutritional supplements. People commencing ART should be given advice on safer sex, including condom use and avoidance of other high-risk activities such as sharing of injecting equipment, to prevent transmitting HIV to other people.

Page 32. Recommendations for initiating antiretroviral therapy: Adults (persons older than 18 years)	These 2016 WHO Guidelines are not included in the national protocol. But on the basis of RP-3493 (the state program for 2018), paragraph 5 includes a step-by-step transition to ART for all PLHIV from the moment of the diagnosis confirmation regardless of the level of CD4 cells: stage 1 is for all younger than 18 years, stage 2 is for all younger than 30, stage 3 is for all PLHIV regardless of age. At the end of 2018, 95% of PLHIV younger than 19 years initiated ART (statistics of the Republican AIDS Center). This limitation (phased approach) was adopted due to financial constraints and unpreparedness of primary health care specialists, as well as insufficient decentralization of treatment services.	**Page 74. When to start ART in adults (>19 years old):** ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count.
Page 32: It is recommended to start ART if the CD4 count is ≤500 cells/mm³ at clinical stages 1 and 2 of HIV, taking into account the patient's desire and willingness to receive ART with adherence.	It does not comply with the 2016 WHO Guidelines. The current national protocol contains the recommendations specified in the 2014 WHO Consolidated Guidelines.	
Page 32: It is recommended to start ART if the HIV VL level is 100,000 copies or higher regardless of clinical and immunological indicators, taking into account the desire and readiness to receive ART with adherence.	It does not comply with the 2016 WHO Guidelines. This recommendation in the national protocol was adapted from the protocol on the HIV treatment of the Russian Federation (2016). The reason for this was the frequent "out-of-stock" situations regarding the CD4 test systems.	
Page 32: Priority initiation of ART for all PLHIV if CD4 count ≤350 cells/mm³. All people with severe HIV or advanced HIV disease (WHO clinical stage 3 or 4), regardless of CD4 count.	It complies with the 2016 WHO Guidelines.	**Pages 74, 78:** As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤350 cells/mm3 (strong recommendation, moderate-quality evidence).
Page 32: ART should be started in all pregnant and breastfeeding women living with HIV regardless of the clinical stage of the disease according to WHO and at any CD4 cell count, and continued life.	It complies with the 2016 WHO Guidelines.	**Page 81:** ART should be initiated in all pregnant and breastfeeding women living with HIV regardless of WHO clinical stage and at any CD4 cell count and continued lifelong.
Page 32: Initiation of ART is recommended regardless of WHO clinical stage or CD4 cell count in all TB patients living with HIV regardless of CD4 cell count. TB treatment should be started first, followed by ART as early as possible within the first 8 weeks of treatment. HIV-positive TB patients with profound immunosuppression (CD4 cell count less than 50 cells/mm3) should receive ART within the first two weeks of initiating TB treatment.	It complies with the 2016 WHO Guidelines.	**Page 93:** ART should be started in all TB patients living with HIV, regardless of CD4 cell count (strong recommendation, high-quality evidence). TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment (strong recommendation, high-quality evidence) HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm3) should receive ART within the first two weeks of initiating TB treatment.
Page 33: ART should be started in everyone regardless of WHO clinical stage or CD4 cell count, considering the willingness and readiness of the parent/guardian to adhere to ART and to give written consent.	It complies with the 2016 WHO Guidelines. The national protocol was amended: taking into account the wishes and readiness of the parent/ guardian to adhere to ART and give written consent. These amendments are an emphasis on healthcare workers to be ready for the monitoring of parents' and guardians' adherence.	**Page 86:** ART should be initiated in all adolescents living with HIV, regardless of WHO clinical stage and at any CD4 cell count.
Page 33: Prioritize ART for all children older than 5 years if CD4 counts ≤350 cells/mm³. Priority ART initiation for all children with severe or advanced HIV disease (WHO clinical stage 3 or 4).	It complies with the 2016 WHO Guidelines.	**Page 86:** As a priority, ART should be initiated in all adolescents with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adolescents with a CD4 count ≤350 cells/mm3 (strong recommendation, moderate-quality evidence).

Page 33. Children aged 1 to 10: ART should be initiated in everyone, regardless of WHO clinical stage or CD4 cell count, considering the parent/guardian's willingness and readiness to adhere to ART and to give written consent. Priority ART is required for all children 5 years and older if CD4 counts ≤350 cells/mm³. Priority initiation of ART for all children with severe or advanced HIV disease (WHO clinical stage 3 or 4). Children aged 1-5 or with a severe or advanced disease caused by HIV (WHO clinical stage 3 or 4), or with a CD4 count ≤750 cells/mm3 or <25% depending on fewer values.	It complies with the 2016 WHO Guidelines.	**Page 89. When to start ART in infants and children younger than 10 years of age:** ART should be initiated in all children living with HIV, regardless of WHO clinical stage or at any CD4 cell count: • Children living with HIV 1 year old to less than 10 years old (conditional recommendation, low-quality evidence). As a priority, ART should be initiated in all children ≤2 years of age or children younger than 5 years of age with WHO clinical stage 3 or 4 or CD4 count ≤750 cells/mm³ or CD4 percentage <25%, and children 5 years of age and older with WHO HIV clinical stage 3 or 4 disease or CD4 count ≤350 cells/mm³
Page 33: ART should be started in any child with active TB disease as soon as possible and within 8 weeks following the start TB treatment regardless of CD4 cell count and clinical stage of the disease.	It complies with the 2016 WHO Guidelines.	**Pages 93, 118:** ART should be started in any child with active TB disease as soon as possible and within 8 weeks following the initiation of antituberculosis treatment, regardless of the CD4 cell count and clinical stage.
Part 2. Diagnostic recommendations		
	These recommendations are not approved by the country. Until now, the 2012 WHO Guidelines on HIV testing are used. The algorithm for making a diagnosis of HIV is based on a 2-double ELISA screening and a confirmatory Western blot method.	**Page XXV:** Principles and Approaches for Service Delivery. Retest all clients diagnosed HIV-positive with a second specimen and a second operator using the same testing strategy and algorithm before enrolling the client in care and/or initiating ART, regardless of whether or not ART initiation depends on CD4 count. Retesting people on ART is not recommended, as there are potential risks of incorrect diagnosis, particularly for in vitro diagnostics (IVDs) that use oral fluid specimens.
Order of the MoH of RUz, No. 336 of 2018, page 72: Some of the information about HIV and VCT can be shared with client groups. At the same time, an individual pre-test consultation should be available to everyone who applies for VCT. Pre-test counseling allows: • help the client/patient to assess the personal risk of HIV infection; • present to the client/patient the testing procedure and the meaning of the test results; • let the client/patient understand the possible consequences to be tested; • help the client/patient make an informed decision about the testing; • raise awareness of the client/patient on HIV/AIDS issues; • form an idea of safe behavior, support • changes in behavior or attempts to make such changes.	The 2016 WHO Guidelines, paragraph 2.4 Principles, and Approaches for Service Delivery refer to the 2007 WHO Guidelines. The current national regulatory document fully complies with the 2007 WHO Guidelines.	**Page XXV:** Principles and Approaches for Service Delivery. Depending on local conditions, pre-test information can be provided in the form of individual information sessions or in group health information talks. Informed consent should always be given individually, in private, in the presence of a health care provider. When recommending HIV testing and counselling to a patient, the health care provider should at a minimum provide the patient with the following information:

Structure of pre-test consultation: 1. Assess the patient's personal risk of HIV infection (information on HIV transmission modes and a link to risk behavior). 2. Assess the level of knowledge and ability to cope with the crisis. · What does the patient know about testing and its benefits? · Why does the patient want to take the test (and does he want to)? · What does the patient know about HIV? · Has the patient thought about the reaction to the different test results? · If the result is positive, who will provide support? 3. Give the patient an overview of HIV/AIDS. 4. Provide information on the testing procedure, possible results, "window period" (here it is important for the consultant to know exactly which test systems are used, since, depending on the sensitivity of the test system, the period when it cannot yet determine the presence of antibodies in the blood can last from 3-4 weeks to 3-4 months.). 5. Discuss potential meaning (personal, medical, social, psychological, legal) of the possible test results. 6. Obtain the written consent/refusal from the patient to take the test. 7. Establish a friendly relationship as a basis for post-test counseling (if the client chose to take the test) or the next call (if the client chose not to take the test).		· The reasons why HIV testing and counselling is being recommended · The clinical and prevention benefits of testing and the potential risks, such as discrimination, abandonment or violence · The services that are available in the case of either an HIV-negative or an HIV-positive test result, including whether antiretroviral treatment is available · The fact that the test result will be treated confidentially and will not be shared with anyone other than health care providers directly involved in providing services to the patient · The fact that the patient has the right to decline the test and that testing will be performed unless the patient exercises that right · The fact that declining an HIV test will not affect the patient's access to services that do not depend upon knowledge of HIV status · In the event of an HIV-positive test result, encouragement of disclosure to other persons who may be at risk of exposure to HIV · An opportunity to ask the health care provider questions.
Order of the MoH of RUz, No. 336 of 2018, page 76: **Services of post-test counseling.** Post-test counseling should be offered for all possible test results. **Counseling for a negative test** is just as important as a positive one. While the client is likely to be relieved and prefers to leave the office as soon as possible, the counselor should try to explain to him the true significance of the experience. It is important to give the client an opportunity to think what he/she thinks about the negative result and to share what he/she can do to stay HIV negative. It is timely to reiterate key messages about safer sexual behavior (condom use, fewer sex partners), and the risks of injecting substance use. It may be worth discussing whether the client is using condoms, and if not, find out the reasons for refusal, provide information on the effectiveness, and correct use of condoms for HIV and STI prevention. **Scheme of post-test counseling in case of a negative result:** Greet the client. Confirm confidentiality guarantees. Remind the patient of the pre-test counseling content. Report the test result and explain the meaning of this result. Make sure the client understands the test result correctly. Ask what the client thought and felt while waiting for the result. Discuss a personal plan of safe behavior/risk reduction. Provide information on services where he/she can go for information, help, and support. Explain the possibility of retesting, the reason why it might be needed. Answer his/her questions and explanations. Remind that the patient, in case of any questions, can always contact this service.	The 2016 WHO Guidelines, paragraph 2.4 Principles and Approaches for Service Delivery refers to the 2007 WHO Guidelines. The current national regulatory document fully complies with the 2007 WHO Guidelines.	**Page XXV:** Principles and Approaches for Service Delivery. Post-test counselling is an integral component of the HIV testing process. All individuals undergoing HIV testing must be counselled when their test results are given, regardless of the test result. Counselling for individuals with HIV-negative test results should include the following minimum information: · An explanation of the test result, including information about the window period for the the appearance of HIV-antibodies and a recommendation to re-test in case of a recent exposure · Basic advice on methods to prevent HIV transmission · Provision of male and female condoms and guidance on their use. · The health care provider and the patient should then jointly assess whether the patient needs referral to more extensive post-test counselling session or additional prevention support, for example, through community -based services.

Order of the MoH of RUz, No. 336 of 2018, page 78: **With a positive result. If the result is positive:** • Briefly remind the patient of the initial consultation; • Explain the results to the patient and give him/her time to think about them; • Make sure the patient understands the essence of the results; • Assess the patient's response to the result and provide psychosocial support; • Assess the patient's understanding of the test results; • Assess the patient's emotional stress associated with the positive result of HIV infection, and identify a person who can support him; • Discuss how the positive result might affect the patient's lifestyle and quality of life; • Emphasize the effectiveness of HIV treatment with ARV drugs; • Determine the period in which the patient should be referred to a healthcare facility; • Inform the patient about psychosocial services, provide information on HIV services, self-help groups and NGOs, their addresses, telephone numbers and how to apply; • Provide information about other infections similar to HIV infection (STIs, viral hepatitis B, C, etc.); • Say about the need to inform the patient's sexual partner about his/her HIV status; • Explain the need to test the patient's sexual partner and children for HIV; • Inform the patient's sexual partner about the need to use personal protective equipment to prevent HIV and STIs; • Inform the patient about the importance of healthcare supervision, as well as the address, work schedule and procedure for referral to the healthcare facility that supervises him/her; • Inform the patient/client that they can be contacted again for further information or advice. Positive HIV test results should focus on the confidentiality of all medical and non-medical services provided to the patient during counseling.	The 2016 WHO Guidelines, paragraph 2.4 Principles and Approaches for Service Delivery refers to the 2007 WHO Guidelines. The current national regulatory document fully complies with the 2007 WHO Guidelines.	**Page XXV:** Principles and Approaches for Service Delivery. In the case of a positive HIV test result, healthcare providers should: • Inform the patient of the result simply and clearly and give the patient time to consider it • Ensure that the patient understands the result • Allow the patient to ask questions • Help the patient to cope with emotions arising from the test result • Discuss any immediate concerns and assist the patient to determine who in her/his social network may be available and acceptable to offer immediate support • Describe follow-up services that are available in the health facility and in the community, with special attention to the available treatment, PMTCT and care and support services • Provide information on how to prevent transmission of HIV, including the provision of male and female condoms and guidance on their use • Provide information on other relevant preventive health measures such as good nutrition, use of co-trimoxazole and, in malarious areas, insecticide-treated bed nets • Discuss possible disclosure of the result, when and how this may happen and to whom • Encourage and offer referral for testing and counselling of partners and children • Assess the risk of violence or suicide and discuss possible steps to ensure the physical safety of patients, particularly women • Arrange a specific date and time for follow-up visits or referrals for treatment, care, counselling, support and other services as appropriate (e.g. tuberculosis screening and treatment, prophylaxis for opportunistic infections, STI treatment, family planning, antenatal care, opioid substitution therapy, and access to sterile needles and syringes).
Testing by non-professional healthcare workers using express diagnostic methods		
National Protocol for Rapid Testing (Order of the MoH of RUz, No. 200), page 7: This National Protocol aims to provide recommendations on the implementation and use of rapid tests for Human Immunodeficiency Virus (HIV) at anonymous consulting rooms to expand access to this service for populations at higher risk of HIV infection. Services include provider-initiated testing and counseling, which includes: • Usual offer of testing for persons receiving medical care in healthcare facilities such as dermatovenerologic, tuberculosis and narcological, antenatal clinics and maternity hospitals; • Institutions offering services for populations with an increased risk of infection in all stages of the epidemic.	It complies with the 2016 WHO Guidelines.	**Page 30:** **Key populations.** HIV testing services should be routinely offered to all key populations in the community, in closed settings such as prisons and in facility-based settings. Community-based HIV testing services for key populations linked to prevention, treatment and care services are recommended, in addition to routine facility-based HIV testing services, in all settings

Testing initiated by a healthcare worker		
The Law of the RUz "On counteracting the spread of the disease caused by the human immunodeficiency virus (HIV)". Article 13. Medical examination for HIV: "Medical examination for HIV of adolescents and persons declared incapable or with limited capacity is conducted with the consent of their legal representatives." **Order of the MoH of RUz, dated May 15, 2014, No. 2584 "On approval of the Rules for conducting the medical examination for the human immunodeficiency virus," paragraph 12:** HIV testing of adolescents and persons declared incapable or with limited capacity is conducted with the consent of their legal representatives.	The national protocol does not have these recommendations, since they contradict the regulations and the law implemented in the country.	**Page 29:** **Provider-initiated HIV testing and counselling for infants and children.** In generalized epidemic settings, infants and children with unknown HIV status who are admitted for inpatient care or attending malnutrition clinics should be routinely tested for HIV. In generalized epidemic settings, infants and children with unknown HIV status should be offered HIV testing in outpatient or immunization clinics.
	The national protocol does not have these recommendations. It is necessary to revise these recommendations in the national protocol.	**Page 47:** **Provider-initiated HIV testing and counselling.** In all settings, children with a parent living with HIV should be routinely offered HIV testing and, if found to be either infected or at high risk of infection through breastfeeding, should be linked to services for treatment or prevention.
Diagnosis of HIV infection in children and infants, in particular, the sensitivity and specificity of tests.		
Order No. 336, page 40: Methods for diagnosing and screening HIV infection in children are determined by the mother's HIV status. Control methods: ELISA and immunoblot. Biological materials used for ELISA and immunoblot analysis: blood and serum specimens. Examination of children in accordance with clinical guidelines is carried out as in adults. If the ELISA test results are positive, it is recommended to repeat the ELISA, as well as to test the parents for HIV by ELISA. In cases of a negative ELISA in the mother, the diagnosis for the infant or child older than 1 year is confirmed by Western blotting.	It partially complies with the 2016 WHO Guidelines. The national protocol does not recommend the use of rapid tests to detect HIV in infants and children. The national protocol and other national recommendations do not contain indications for the use of the rapid diagnostic tests for HIV serology in children.	**Page 29:** HIV-exposure status in infants and children 4–18 months of age should be ascertained by undertaking HIV serological testing in the mother. Rapid diagnostic tests for HIV serology can be used at 9 months to rule out HIV infection in asymptomatic HIV-exposed infants. Rapid diagnostic tests for HIV serology can be used to diagnose HIV infection in children older than 18 months following the national testing strategy. Addition of nucleic acid testing (NAT) at birth to existing early infant diagnosis (EID) testing approaches can be considered to identify HIV infection in HIV-exposed infants.
Order No. 277, page 302: The first PCR test for HIV DNA should be **performed in a child aged 6-8 weeks.** One-time positive and/or negative HIV DNA PCR results require confirmation. Confirmation of a positive HIV DNA PCR test result is carried out by the same method in a separate blood specimen as soon as possible (preferably within 5-7 days after receiving the first result) and, preferably, in the same laboratory. Two positive HIV DNA PCR results indicate that the child is infected with HIV and requires immediate clinical examination for the optimal choice of the infant's ART regimen. In case of a negative HIV DNA PCR result at the age of 6-8 weeks, the infant should be re-examined at the age of 12 weeks. Two negative HIV DNA PCR results (at 6 and 12 weeks of age) allow the child to be considered not infected if it is not breastfed. In case of negative results in a newborn who has been in contact with HIV (by PCR), an ELISA test for antibodies to HIV is performed at the age of 18 months to detect seroconversion. **Order No. 277, page 33:** ART should be started in all infants, regardless of WHO clinical stage or CD4 cell count. The initiation of ART is recommended for all children under 18 months of age with a presumptive clinical diagnosis of HIV infection (taking into account a double positive DNA PCR result).	It complies with the 2016 WHO Guidelines.	**Page 29:** It is strongly recommended that HIV virological testing be used to diagnose HIV infection in infants and children below 18 months of age. It is strongly recommended that all **HIV-exposed infants have HIV virological testing at 4–6 weeks** of age or at the earliest opportunity thereafter. In infants with an **initial positive virological test result, it is strongly recommended that ART be started without delay** and, at the same time, a second specimen is collected to confirm the initial positive virological test result. Do not delay ART. Immediate initiation of ART saves lives and should not be delayed while waiting for the results of the confirmatory test.

Order No. 277, page 302: In children under 18 months, including newborns, the gold standard for diagnosing HIV infection is the molecular genetic method for determining HIV DNA (HIV DNA PCR). A PCR test for HIV proviral DNA is performed twice at 6 and 12 weeks of age. If the newborn has been exposed to HIV late in the prenatal period due to late mother's appeal, treatment failure or her low adherence to treatment, or if the child has signs of HIV at birth, an early HIV test (HIV pro-viral DNA PCR) is recommended during the first week of a baby's life.	The national protocol does not contain these recommendations. All HIV-exposed infants younger than 6 months undergo double pro-viral DNA PCR. In case of a positive result, ART is immediately prescribed. ELISA for HIV-exposed infants is carried out at the age of 18 months if the child was formula-fed.	**Page 29:** It is strongly recommended that HIV-exposed infants who are well undergoing HIV serological testing at around 9 months of age (or at the time of the last immunization visit). Infants who have reactive serological assays at 9 months should have a virological test to identify HIV infection and the need for ART.
Testing in special groups (adolescents, pregnant women, couples, and partners).		
The Law of the RUz "On counteracting the spread of the disease caused by the human immunodeficiency virus (HIV)." Article 13. Medical examination for HIV: "Medical examination for HIV of adolescents and persons declared incapable or with limited capacity is carried out with the consent of their legal representatives" **Order of the MoH of RUz, dated May 15, 2014, No. 2584 "On approval of the Rules for conducting the medical examination for the human immunodeficiency virus," paragraph 12:** HIV testing of adolescents and persons declared incapable or with limited capacity is conducted with the consent of their legal representatives.	The national protocol does not have these 2016 WHO Guidelines. These Guidelines contradict the legislative act adopted for the use in the national protocol.	**Page 29:** **Adolescents.** HIV testing services, with linkages to prevention, treatment and care, should be offered for adolescents from key populations in all settings. Adolescents with HIV should be counselled about the potential benefits and risks of disclosure of their HIV status and empowered and supported to determine if, when, how and to whom to disclose. **Generalized HIV epidemic:** HIV testing services with linkage to prevention, treatment and care should be offered to all adolescents in generalized epidemics. **Concentrated HIV epidemic:** HIV testing services with linkage to prevention, treatment and care should be accessible to adolescents in low-level and concentrated epidemics.
Order No. 137, dated May 18, 2012, "On the organization and provision of antenatal care and medical care for pregnant women in primary health care institutions": · Ensuring 100% coverage of HIV counseling and testing of pregnant women; · Provision of full-fledged postpartum care, counseling, including the implementation of postpartum contraception, 40-45 days after childbirth. **Order No. 277, page 310:** HIV infection: principles of testing and counseling. Human immunodeficiency virus (HIV) testing and counseling should be offered to clients and their partners under the following circumstances: · Diagnosis or treatment of STIs and other infections of the reproductive tract (RTI); · Counseling on contraception (emphasize that it is important to know your HIV status when choosing a contraceptive method); · Planning a pregnancy (to minimize the risk of MTCT); · Antenatal care (to properly plan the management of pregnancy and childbirth and prevent MTCT); · Monitoring the newborn (to choose a safe feeding method if the mother's HIV status is unknown); · Counseling about unwanted pregnancy; · Screening for cervical cancer.	It complies with the 2016 WHO Guidelines.	**Page 30:** **Pregnant women. High prevalence settings:** PITC for women should be considered a routine component of the package of care in all antenatal, childbirth, postpartum and paediatric care settings.

	The national protocol does not have this. There are also no such recommendations in other current regulatory documents in the country.	**Page 30:** **Pregnant women. High prevalence settings:** In such settings, where breastfeeding is the norm, lactating mothers who are HIV negative should be retested periodically throughout the period of breastfeeding.
Order No. 137, Annex 3, page 10. **The standard for the management and examination of women with physiological pregnancy.** At the 1st examination of a pregnant woman it is necessary (pregnancy up to 12 weeks) to order the following tests: blood for syphilis - RW, hepatitis B and C, for HIV/AIDS, general blood, blood group and Rh factor, blood for sugar, general urine, urethra, vagina, and cervix discharge tests, stool analysis for parasites.	Contrary to the 2016 WHO guidelines, all HIV-negative pregnant women should be screened for HIV in the first trimester of pregnancy. After childbirth and / or during childbirth, HIV tests are carried out in cases where the pregnant woman did not undergo an HIV ELISA test in the first trimester of pregnancy.	**Page 30:** **Pregnant women. High prevalence settings:** All HIV-negative pregnant women should be retested in the third trimester, postpartum and/ or during labour, because of the high risk of acquiring HIV during pregnancy.
Order No. 137, dated May 18, 2012, "On the organization and provision of antenatal care and medical care for pregnant women in primary health care institutions": · Ensuring 100% coverage of HIV counseling and testing of pregnant women; · Provision of full-fledged postpartum care, counseling, including the implementation of postpartum contraception, 40-45 days after childbirth. **Order No. 137, Annex 3, page 10:** The standard for the management and examination of women with physiological pregnancy. At the 1st examination of a pregnant woman it is necessary (pregnancy up to 12 weeks) to order the following tests: blood for syphilis - RW, hepatitis B and C, for HIV/AIDS, general blood, blood group and Rh factor, blood for sugar, general urine, urethra, vagina, and cervix discharge tests, stool analysis for parasites.	It complies with the 2016 WHO Guidelines.	**Page 30:** **Pregnant women. Low prevalence settings:** PITC can be considered for pregnant women in antenatal care as a key component of the effort: · to eliminate mother-to-child transmission of HIV · to integrate HIV testing with other key testing (for viral hepatitis, syphilis, etc.) as relevant to the setting
Order No. 277, page 240: In all studies of pre-exposure prophylaxis of HIV, it is provided in comprehensive measures for HIV prevention: · Regular HIV testing and counseling, · Provision of personal protective equipment, · Screening and treatment of sexually transmitted infections (STIs), · Adherence counseling and other methods that are effective for a particular population.	It complies with the 2016 WHO Guidelines.	**Page 30:** **Pregnant women. Low prevalence settings:** Retesting HIV negative pregnant women who are in a serodiscordant couple, from a key population group or have known ongoing HIV risk.
	There are no such recommendations in national protocols. It would be good if national consultants included these 2016 WHO Guidelines and, in addition, developed information and educational materials, and disseminated them in anonymous consulting rooms for risk groups and those who are tested for HIV anonymously and regularly.	**Page 30:** **Couples and partners.** Couples and partners should be offered voluntary HIV testing services with support for mutual disclosure. This applies also to couples and partners from key populations (strong recommendation, low-quality evidence). In antenatal care settings, couples and partners should be offered voluntary HIV testing services with support for mutual disclosure (strong recommendation, low-quality evidence). HIV testing services for couples and partners, with support for mutual disclosure, should be offered to individuals with known HIV status and their partners.

Order No. 277, page 24: Determination of the CD4 count is necessary to: establish the stage (immunological category) of HIV infection; establish indications for initiating and canceling preventive treatment for opportunists; establish indications for starting ART; track immunological response to ART (CD4 recovery during treatment).	It complies with the 2016 WHO Guidelines.	**Page 44:** **CD4 cell count testing at the point of care.** CD4 cell count testing at the point of care can be used to prioritize patients for urgent linkage to care and ART initiation.
Diagnostic algorithms		
Order No. 336, page 40: **Diagnostic algorithm. First screening:** Tests for detecting antibodies to HIV by ELISA are carried out by district, inter-district, regional, city, and republican diagnostic laboratories. If the result is positive, they are **re-examined** using ELISA. A second sample is also being considered at the district level. If the result is positive, the sera are examined **by the method of immune blotting** at the regional and Republican AIDS Centers. **Only in the case of a positive immune blot, the patient is registered in the HIV health care system. Only patients with positive IB are accepted on ART.**	It does not comply with the 2016 WHO Guidelines.	**Page 19:** **Retest before starting treatment.** National programs should retest all newly diagnosed and previously diagnosed HIV-positive people before enrolling in HIV health care. Retesting people on ART is not recommended, as there are potential risks of incorrect diagnosis, particularly for in vitro diagnostics (IVDs) that use oral fluid specimens.
Part 3. ARV drugs for HIV prevention		
Pre-exposure prophylaxis of HIV infection		
Order No. 277, page 240: ART should be offered to HIV-negative partners in serodiscordant couples to reduce possible virus transmission to uninfected partners. PrEP consisted of TDF/3TC (300/150 mg) or TDF/FTC 300/200 mg per 1 tablet daily orally may be considered an option to protect an uninfected partner in serodiscordant couples during conception.	It complies with the 2016 WHO Guidelines.	**Page 32:** Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches.
Page 33: HIV in serodiscordant couples. It is recommended to start ART regardless of the WHO clinical stage of the disease for partners with HIV in serodiscordant couples (to reduce the risk of HIV transmission), taking into account the willingness and readiness to take ART with adherence. **Page 240:** **PrEP regimen.** TDF/3TC (300/150 mg) or TDF/FTC (300/200 mg) 1 tablet orally daily.	It complies with the 2016 WHO Guidelines, but the TDF/3TC combination is used.	**Page 32:** Oral pre-exposure prophylaxis of HIV infection. Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk1 of HIV infection as part of combination HIV prevention approaches.
Order No. 277, page 310: HIV testing and counseling should be offered to clients and their partners, as well as contraception counseling, pregnancy planning, antenatal care, newborn monitoring, and unwanted pregnancy counseling. It is necessary that every person with HIV who sought SRH services should receive appropriate counseling. Recommendations on contraception should be individualized, tailored to the needs of each woman or couple, and take into account the stage of HIV infection, treatment, lifestyle, and personal preferences.	It complies with the 2016 WHO Guidelines.	**Page 60:** **Pregnancy.** Contraception services, safer conception management and links to antenatal care should be available when providing PrEP services for women. The risks and benefits of and alternatives to continuing to use PrEP during pregnancy and breastfeeding should be discussed with each person.

Algorithm and regimens of post-exposure prophylaxis for different population groups, including PMTCT.		
Order No. 277, page 226: A regimen of three ARV drugs (two NRTIs and one protease inhibitor - PI) is recommended for the course of PEP. Preferred regimen: TDF + 3TC + LPV/r. Alternative regimen: AZT + 3TC + LPV r (ATV/r). HIV PEP regimens for children ≤ 10 years. Preferred regimen: AZT + 3TC + LPV r. Alternative regimen: ABC + 3TC or TDF + 3TC. LPV/r or ATV/r may be included as a third drug according to the weight of the child. PEP duration is 4 weeks (28 days).	It complies with the 2016 WHO Guidelines.	**Page 32:** A regimen for post-exposure prophylaxis for HIV with two drugs is effective, but three drugs are preferred (conditional recommendation, very low-quality evidence). Post-exposure prophylaxis ARV regimens for adults and adolescents: TDF + 3TC (or FTC) is recommended as the preferred backbone2 regimen for HIV post-exposure prophylaxis in adults and adolescents (strong recommendation, low-quality evidence). LPV/r or ATV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for adults and adolescents (conditional recommendation, very low-quality evidence). Where available, RAL, DRV/r or EFV can be considered as alternative options. Post-exposure prophylaxis ARV regimens for children ≤10 years: AZT + 3TC is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis for children aged 10 years and younger. ABC + 3TC or TDF + 3TC (or FTC) can be considered as alternative regimens (strong recommendation, low-quality evidence). LPV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for children younger than 10 years (conditional recommendation, very low-quality evidence). An age-appropriate alternative regimen can be identified among ATV/r, RAL, DRV, EFV and NVP. A full 28-day prescription of antiretroviral drugs should be provided for HIV post-exposure prophylaxis following initial risk assessment
Order No. 277, page 289: ART should be initiated for all pregnant and breastfeeding women living with HIV regardless of WHO clinical stage of and at any CD4 cell count, and continued lifelong.	It complies with the 2016 WHO Guidelines.	**Page 81:** ART should be initiated in all pregnant and breastfeeding women living with HIV regardless of WHO clinical stage and at any CD4 cell count and continued lifelong.
Order No. 277, page 296: If VL was not determined before childbirth (at 34-36 weeks of gestation), the elective caesarian section is performed at 38 weeks (if there are no obstetric contraindications to ECS).	It does not comply with the 2016 WHO Guidelines. In the country, 98% of babies born to HIV-positive women are born healthy. Viral load tests among pregnant women with HIV are performed at 34-36 weeks of gestation and 87% of pregnant women with HIV have VL of the undetectable level. The national recommendations should be amended to use ECS in cases of strict indications by obstetricians-gynecologists or with high VL.	**Page 104:** Although the elective caesarean section has been shown to protect against HIV acquisition, especially in the absence of ARV drugs or in the case of a high viral load, WHO does not recommend it in resource-limited settings specifically for HIV infection; rather, it is recommended for obstetric and other medical indications.

Order No. 277, page 296: **Newborn management:** in case of breastfeeding the infant for 6 months by the mother receiving ART for the entire breastfeeding period and if the infant takes NVP for 6–12 weeks. **Page 304:** **The NCP presents several scenarios:** If the mother has the HIV diagnosis during pregnancy and she plans to breastfeed her baby, it is prescribed a 6-week course of NVP. If the mother has HIV after delivery but no later than or after 48 hours, the baby is breastfed, the baby is prescribed a 12-week course of NVP. If the mother discontinues ART, the infant continues or resumes NVP for the entire breastfeeding period and for an additional 6 weeks after the mother restarts ART or up to 1 week after breastfeeding is stopped.	It complies with the 2016 WHO Guidelines.	**Page 120:** · Infants born to mothers with HIV who are at high risk of acquiring HIV should receive dual prophylaxis with AZT (twice daily) and NVP (once daily) for the first 6 weeks of life, whether they are breastfed or formula-fed (strong recommendation, moderate-quality evidence). · Breastfed infants who are at high risk of acquiring HIV, including those first identified as exposed to HIV during the postpartum period, should continue infant prophylaxis for an additional 6 weeks (total of 12 weeks of infant prophylaxis) using either AZT (twice daily) and NVP (once daily) or NVP alone (conditional recommendation, low-quality evidence). · Infants of mothers who are receiving ART and are breastfeeding should receive 6 weeks of infant prophylaxis with daily NVP. If infants are receiving replacement feeding, they should be given 4–6 weeks of infant prophylaxis with daily NVP (or twice-daily AZT) (strong recommendation, moderate-quality evidence for breastfeeding infants; strong recommendation, low-quality evidence for infants receiving only replacement feeding).
Part 4. Antiretroviral therapy regimens		
When ART should be started, including recommendations for specific groups of patients (for whom urgent indication is recommended).		
Page 32: **Recommendations on initiating antiretroviral therapy.** **Adults (persons older than 18 years):** It is recommended to start ART if the CD4 count is ≤500 cells/mm³ at HIV clinical stages 1 and 2, taking into account the patient's willingness and readiness to receive ART and adherence to treatment. It is recommended to start ART if the VL HIV level is 100,000 copies or higher regardless of clinical and immunological indicators, taking into account the willingness and readiness to receive ART and adherence to treatment. Priority initiation of ART for all PLHIV if CD4 count ≤350 cells/mm³. All people with severe HIV or advanced HIV disease (WHO clinical stage 3 or 4) are regardless of CD4 count.	It complies with the 2016 WHO Guidelines.	**Page 33:** **Clinical guidelines: antiretroviral therapy.** **When to start ART in adults (> 19 years old):** ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count. As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with a CD4 count ≤350 cells/mm3.
Page 32: **Pregnant PLHIV:** ART should be started in all pregnant and breastfeeding women living with HIV regardless of the WHO clinical stage and any CD4 cell count, and treatment should be continued lifelong.	It complies with the 2016 WHO Guidelines.	**Page 33:** **When to start ART in pregnant and breastfeeding women:** ART should be initiated in all pregnant and breastfeeding women living with HIV, regardless of WHO clinical stage and at any CD4 cell count and continued lifelong.
Page 32: **Adolescents (≥10 years):** ART should be initiated in everyone regardless of WHO clinical stage or CD4 cell count, taking into account the parent's/ guardian's willingness and readiness to adhere to ART and to give written consent.	It complies with the 2016 WHO Guidelines.	**Page 33:** **When to start ART in adolescents (10-19 years of age):** ART should be initiated in all adolescents living with HIV, regardless of WHO clinical stage and at any CD4 cell count (conditional recommendation, low-quality evidence). As a priority, ART should be initiated in all adolescents with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adolescents with a CD4 count ≤350 cells/mm3.

Page 32: **Children aged 5 to 10 years:** ART should be initiated in everyone regardless of the WHO clinical stage of the disease or the CD4 cell count, taking into account the parent's/guardian's willingness and readiness to adhere to ART and to give written consent. Priority ART is required for all children older than 5 years if CD4 counts ≤350 cells/mm³. Priority initiation of ART is for all children with severe or advanced HIV disease (WHO clinical stage 3 or 4). **Children 1–5 years of age:** ART should be initiated in everyone regardless of WHO clinical stage or CD4 cell count, taking into account the parent's/guardian's willingness and readiness to adhere to ART and to give written consent. Priority initiation of ART for all children living with HIV, aged 1–5 years or with severe/advanced HIV disease (WHO clinical stage 3 or 4), or CD4 count ≤750/mm3 or <25%, depending on which value is less. **Infants <1 year:** ART should be initiated for all infants regardless of the WHO clinical stage or CD4 cell count.	It complies with the 2016 WHO Guidelines.	**Page 33:** **When to start ART in children younger than 10 years of age:** ART should be initiated in all children living with HIV, regardless of WHO clinical stage or at any CD4 cell count. Infants diagnosed in the first year of life. Children living with HIV 1 year old to less than 10 years old. As a priority, ART should be initiated in all children <2 years of age or children younger than 5 years of age with WHO clinical stage 3 or 4 or CD4 count ≤750 cells/mm³ or CD4 percentage <25% and children 5 years of age and older with WHO clinical stage 3 or 4 or CD4 count ≤350 cells/mm³ (strong recommendation, moderate-quality evidence)
Page 32: **HIV patients with TB:** ART is recommended to be started regardless of the WHO clinical stage or CD4 cell count in all TB patients living with HIV regardless of CD4 cell count. TB treatment should be started first, followed by ART as soon as possible during the first 8 weeks of treatment. HIV-positive TB patients who are profoundly immunosuppressed (CD4 cell count less than 50 cells/mm3) should receive ART within the first two weeks from the start of TB treatment. ART should be initiated in any child with active TB disease as soon as possible and within 8 weeks from the start of TB treatment regardless of CD4 cell count and clinical stage.	It complies with the 2016 WHO Guidelines.	**Page 33:** **Timing of ART for adults and children with TB:** ART should be started in all TB patients living with HIV regardless of CD4 count. TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment. HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/ mm3) should receive ART within the first two weeks of initiating TB treatment. ART should be started in any child with active TB disease as soon as possible and within 8 weeks following the initiation of antituberculosis treatment regardless of the CD4 cell count and clinical stage.
Order No. 277, page 34: **Preferred first-line regimens for adults:** TDF + 3TC (or FTC) + EFV.	It complies with the 2016 WHO Guidelines.	**Page 97:** **Preferred first-line regimens for adults:** TDF + 3TC (or FTC) + EFV.
Order No. 277, page 34: **Alternative first-line regimens for adults:** AZT + 3TC + EFV (or NVP); TDF + 3TC (or FTC) + DTG; TDF + 3TC (FTC) + NVP.	It complies with the 2016 WHO Guidelines.	**Page 97:** **Alternative first-line regimens for adults:** AZT + 3TC + EFV (or NVP); TDF + 3TC (or FTC) + DTG; TDF + 3TC (or FTC) + EFV400; TDF + 3TC (or FTC) + NVP.
Order No. 277, page 34: **Preferred first-line regimens for pregnant or breastfeeding women:** TDF + 3TC (or FTC) + EFV.	It complies with the 2016 WHO Guidelines.	**Page 97:** **Preferred first-line regimens for pregnant or breastfeeding women:** TDF + 3TC (or FTC) + EFV.
Order No. 277, page 34: **Alternative first-line regimens for pregnant or breastfeeding women:** AZT + 3TC + EFV (or NVP); TDF + 3TC (or FTC) + NVP.	It complies with the 2016 WHO Guidelines.	**Page 97:** **Alternative first-line regimens for pregnant or breastfeeding women:** AZT + 3TC + EFV (or NVP); TDF + 3TC (or FTC) + NVP.
Order No. 277, page 34: **Preferred first-line regimens for adolescents:** TDF + 3TC (or FTC) + EFV.	It complies with the 2016 WHO Guidelines.	**Pages 97, 106:** **Preferred first-line regimens for adolescents:** TDF + 3TC (or FTC) + EFV.

Order No. 277, page 34: **Alternative first-line regimens for adolescents:** AZT + 3TC + EFV (or NVP); TDF + 3TC (or FTC) + DTG; TDF (or ABC) + 3TC (FTC) + NVP.	The discrepancy between regimens: TDF (or ABC) + 3TC (or FTC) + EFV400 regimen is absent in the national protocol.	**Page 97:** **Alternative first-line regimens for adolescents:** AZT + 3TC + EFV (or NVP); TDF (or ABC) + 3TC (or FTC) + DTG; TDF (or ABC) + 3TC (or FTC) + NVP.
Order No. 277, page 34: **Preferred first-line regimens for children 3 to 10 years:** ABC + 3TC + EFV .	It complies with the 2016 WHO Guidelines.	**Page 97:** **Preferred first-line regimens for children 3 years to less than 10 years:** ABC + 3TC + EFV.
Order No. 277, page 34: **Alternative first-line regimens for children 3 to 10 years:** ABC + 3TC + NVP; AZT + 3TC + EFV (or NVP); TDF + 3TC (or FTC) + EFV (or NVP).	It complies with the 2016 WHO Guidelines.	**Page 97:** **Alternative first-line regimens for children 3 years to less than 10 years:** ABC + 3TC + NVP; AZT + 3TC + EFV (or NVP); TDF + 3TC (or FTC) + EFV (or NVP).
Order No. 277, page 34: **Preferred first-line regimens for children younger than 3 years:** ABC (or AZT) + 3TC + LPV/r.	It complies with the 2016 WHO Guidelines.	**Page 97:** **Preferred first-line regimens for children less than 3 years:** ABC (or AZT) + 3TC + LPV/r.
Order No. 277, page 34: **Alternative first-line regimens for children younger than 3 years:** ABC (or AZT) + 3TC + NVP .	It complies with the 2016 WHO Guidelines.	**Page 97:** **Alternative first-line regimens for children less than 3 years:** ABC (or AZT) + 3TC + NVP.
Choice of first-line drugs, including: · Preferences for fixed-dose combination (FDCs) drugs. · Refusal to use stavudine. · Use of DTG and EFV400 following the updated recommendations (2018, 2019). · Recommendations for use of dolutegravir in women of childbearing age and pregnant women.		
Order No. 277, pages 34, 72, 97: **Selection of preferred first-line drugs for adults:** Fixed-dose combinations and single daily dosing regimens are preferred for antiretroviral therapy, EFV/TDF/3TC (FDC).	It complies with the 2016 WHO Guidelines.	**Page 98:** **Selection of preferred first-line drugs for adults:** TDF + 3TC (or FTC) + EFV as a fixed-dose combination is recommended as the preferred option to initiate ART.
Order No. 277, pages 34, 71, 72, 76, 77: **Selecting the preferred drugs in alternative first-line regimens for adults in fixed combinations:** 3TC/ZDV (FDC); TDF/3TC (FDC); TDF + 3TC (or FTC) + DTG (FDC); TDF + 3TC + EFV 600 (FDC).	It complies with the 2016 WHO Guidelines, except for EFV 400.	**Pages 98,106:** **Selecting the preferred drugs in alternative first-line regimens for adults in fixed combinations:** 3TC/ZDV (FDC); TDF/3TC (FDC); TDF + 3TC (or FTC) + DTG (FDC); TDF + 3TC (or FTC) + EFV 400.
	Since 2013, stavudine has been removed from treatment regimens.	**Page 98:** All countries should discontinue d4T use in first-line regimens because of its well-recognized metabolic toxicities (strong recommendation, moderate-quality evidence)
Order No. 277, page 34: **The use of DTG is noted in an alternative first-line therapy regimen:** TDF/3TC/DTG (FDC).	1. DTG is used in the national protocol as an alternative line. 2. FDC DTG with TDF and 3TC is used. This is in line with the 2018 Guidelines. 3. EFV400 is not used or purchased in the country, which does not comply with the WHO Guidelines from 2016-2018.	**Page 98:** TDF + 3TC (or FTC) + EFV 400 mg/day may be used as alternative options to initiate ART.

Order No. 277, page 62: There are limited data on the safety of INSTI during pregnancy and breastfeeding. In particular, the safety of DTG during pregnancy is not clearly established. In addition, calcium and iron often used as supplements during pregnancy can significantly reduce the amount of DTG in the body. In the absence of well-controlled studies in pregnant women, DTG and RAL should be used only if the expected benefits outweigh the risks.	The recommendations of the national protocol on the use of DTG for women of childbearing age and pregnant women are broader than those in the 2016 WHO Guidelines.	**Page 98:** Safety and efficacy data on the use of DTG in pregnant women and breastfeeding women are not yet available.
Order No. 277, page 67: Rifampicin is known to significantly reduce plasma DTG concentrations, which may require a twice daily dose increase. The number of studies, however, is extremely small, and clinical experience with this combination is very limited, especially in HIV-infected patients with active TB.	It complies with the 2016 WHO Guidelines.	**Page 98:** Safety and efficacy data on DTG and TB coinfection are still pending (WHO 2016 recommendation).
First-line ART for special patient groups.		
Order No. 277, page 44: For HIV-positive children three years or older but less than 10 years (weight is less than 35 kg), the two NRTI base for the ART regimen should be one of the following combinations in the following preferred order: · ABC + 3TC; · AZT + 3TC.	The national protocol does not recommend the use of TDF in children younger than 10 years.	**Page 109:** For children 3 to less than 10 years of age, the NRTI backbone should be one of the following (in preferential order): · ABC + 3TC; · AZT or TDF + 3TC (or FTC).
Order No. 277, page 44: For HIV-positive children three years and older, EFV is the preferred NNRTI for first-line treatment and NVP is the alternative drug.	It complies with the 2016 WHO Guidelines.	**Page 109:** For children 3 years and older, EFV is the preferred NNRTI for first-line treatment and NVP is the preferred alternative.
Order No. 277, page 43: In children younger than 3 years, the backbone NRTI combination should include ABC (priority) or AZT + 3TC. For first-line ART, all HIV-infected children younger than 3 years (36 months) should use an LPV r-based regimen regardless of NNRTI used by the mother (perinatal contact). If LPV/r is not possible, treatment should be initiated with an NVP-based regimen. If the viral load can be monitored, the substitution LPV/r for EFV after sustained virologic suppression may be considered in 3-year children.	It complies with the 2016 WHO Guidelines.	**Page 113:** For infants and children younger than 3 years, the NRTI backbone for an ART regimen should be ABC or AZT + 3TC. An LPV/r-based regimen should be used as first-line ART for all children infected with HIV younger than 3 years (36 months) of age, regardless of NNRTI exposure. If LPV/r is not feasible, treatment should be initiated with an NVP-based regimen. Where viral load monitoring is available, consideration can be given to substituting LPV/r with EFV at 3 years of age after viral suppression is sustained.
Order No. 277, page 44: In HIV-infected infants and children younger than 3 years, ABC + 3TC + AZT is recommended as a treatment option for children who develop TB while on ART regimen containing NVP or LPV/r and require rifampicin. Once rifampicin therapy is completed, this 3NRTI regimen should be discontinued and the initial ART regimen should be restarted.	It complies with the 2016 WHO Guidelines.	**Page 113:** For infants and children infected with HIV younger than 3 years, ABC + 3TC + AZT is recommended as an option for children who develop TB while on an ART regimen containing NVP or LPV/r. Once TB therapy has been completed, this regimen should be stopped and the initial regimen should be restarted.

Order No. 277, page 34: **Children younger than 3 years.** 1. **1. Preferred regimen for children:** ABC (or AZT) + 3TC + LPV/r. 2. **2. Alternative option:** ABC (or AZT) + 3TC + NVP. 3. **3. Special circumstances:** ABC or AZT + 3TC + RAL.	The national protocol does not contain this step-by-step scenario of treatment regimens for HIV-infected newborns who begin treatment at the time of birth; more precisely, the scenario is generalized with the scenario for children younger than 3 years.	**Page 117:** **The sequence of ARV formulations for newborns starting treatment at around birth.** 1. Preferred regimen for children: · from 0 to 2 weeks: AZT + 3TC + NVP; · from 2 weeks to 3 months: ABC or AZT + 3TC + LPV/r syrup; · from 3 months to 36 months: ABC or AZT + 3TC + LPV/r pellets. 2. Alternative option: · from 0 to 2 weeks: AZT + 3TC + NVP; · from 2 weeks to 3 months: AZT + 3TC + NVP; · from 3 months to 36 months: ABC or AZT + 3TC + LPV/r pellets. 3. Special circumstances: · from 0 to 2 weeks: AZT + 3TC + NVP; · from 2 weeks to 3 months: AZT + 3TC + NVP; · from 3 months to 36 months: ABC or AZT + 3TC + RAL.
Order No. 277, page 34: **ART while TB / HIV co-infection.** ART should be initiated in all TB patients living with HIV regardless of CD4 cell count. TB treatment should be started first, followed by ART as soon as possible during the first 8 weeks of treatment. HIV-positive TB patients who are profoundly immunosuppressed (CD4 cell count less than 50 cells/mm3) should receive ART within the first two weeks of starting TB treatment. ART should be started in a child with active TB disease as early as possible and within 8 weeks of starting a TB treatment, regardless of CD4 cell count and clinical stage of the disease.	It complies with the 2016 WHO Guidelines.	**Page 93:** ART should be started in all TB patients living with HIV, regardless of CD4 cell count (strong recommendation, high-quality evidence). TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment (strong recommendation, high-quality evidence). HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm3) should receive ART within the first two weeks of initiating TB treatment. ART should be started in any child with active TB disease as soon as possible and within 8 weeks following the initiation of antituberculosis treatment, regardless of the CD4 cell count and clinical stage
Order No. 277, page 35: Recommended first-line ARV combination for adult patients on anti-TB treatment: TDF/3TC/EFV or TDF/FTC/EFV. Alternative regimens for TB in adults: PI + TDF / 3TC or FTC, using rifabutin instead of rifampicin.	It complies with the 2016 WHO Guidelines.	**Page 15:** Recommended first-line ARV combination for patients on anti-TB drugs: TDF/FTC/EFV, ABC/3TC/EFV or TDF/FTC/RAL. Alternatives: PI/r + TDF FTC, using rifabutin instead of rifampicin
Order No. 277, page 46: Summary of recommended ART regimens for children who need TB treatment. Younger than 3 years: triple NRTI (AZT + 3TC + ABC); 3 years and older: two NRTIs + EFV or triple NRTI (AZT + 3TC + ABC).	It complies with the 2016 WHO Guidelines.	**Page 119:** Summary of recommended ART regimens for children who need TB treatment. Younger than 3 years: triple NRTI (AZT + 3TC + ABC); 3 years and older: two NRTIs + EFV or triple NRTI (AZT + 3TC + ABC).

Order No. 277, page 46: Recommended regimens for children and infants initiating TB treatment while receiving ART with two NRTIs + EFV or NVP: **Younger than 3 years:** Continue NVP, ensuring that the dose is 200 mg/m2 or triple NRTI (AZT + 3TC + ABC); **3 years and older:** If the child is receiving EFV, continue the same regimen, if the child is receiving NVP, substitute with EFV or triple NRTI (AZT + 3TC + ABC).	It complies with the 2016 WHO Guidelines.	**Page 119:** Recommended regimens for children and infants initiating TB treatment while receiving ART with two NRTIs + EFV or NVP: **Younger than 3 years:** Continue NVP, ensuring that the dose is 200 mg/m2 or triple NRTI (AZT + 3TC + ABC); **3 years and older:** If the child is receiving EFV, continue the same regimen, if the child is receiving NVP, substitute with EFV or triple NRTI (AZT + 3TC + ABC).
Order No. 277, page 46: Children receiving a standard PI-based regimen (two NRTIs + LPV/r). **Younger than 3 years:** triple NRTI (AZT + 3TC + ABC) or continue LPV/r, adding RTV to achieve the full therapeutic dose; **3 years and older:** If the child has no history of failure of an NNRTI-based regimen: substitute with EFV or triple NRTI (AZT + 3TC + ABC) or continue LPV/r, adding RTV to achieve the full therapeutic dose. If the child has a history of failure of an NNRTI-based regimen: triple NRTI (AZT + 3TC + ABC) or continue LPV/r, adding RTV to achieve the full therapeutic dose: increase RTV until it reaches the same dose as LPV in mg, in a ratio of 1:1.	It complies with the 2016 WHO Guidelines.	**Page 119:** Children receiving a standard PI-based regimen (two NRTIs + LPV/r). **Younger than 3 years:** triple NRTI (AZT + 3TC + ABC) or continue LPV/r, adding RTV to achieve the full therapeutic dose; **3 years and older:** If the child has no history of failure of an NNRTI-based regimen: substitute with EFV or triple NRTI (AZT + 3TC + ABC) or continue LPV/r, adding RTV to achieve the full therapeutic dose. If the child has a history of failure of an NNRTI-based regimen: triple NRTI (AZT + 3TC + ABC) or continue LPV/r, adding RTV to achieve the full therapeutic dose: increase RTV until it reaches the same dose as LPV in mg, in a ratio of 1:1.
Order No. 277, page 290: ART should be started in all pregnant and breastfeeding women living with HIV, regardless of the WHO clinical stage and for any CD4 cell count, and treatment should be continued lifelong.	It complies with the 2016 WHO Guidelines.	**Page 120:** **Prevention in infants.** In settings with a high risk of mother-to-child transmission, in addition to providing additional prophylaxis for the infant, ART should be initiated urgently in all pregnant and breastfeeding women, even if they are identified late in pregnancy or postpartum, because the most effective way to prevent mother-to-child HIV transmission is to reduce maternal viral load.
Recommendations for breastfeeding of babies.		
Order No. 277, page 304: ARV in a newborn should be initiated as soon as possible, always in the first 4 hours of life. **Order No. 277, page 294:** Newborn tactics. Three-component ARV prophylaxis is prescribed: Orally (syrups) in the first 4 hours of life: ZDV 50 mg/5ml at a dose of 4 mg/kg (single) every 12 hours for 4 weeks + 3TC 10 mg/ml at a dose of 2 mg/kg (single) every 12 hours within 4 weeks + NVP 50mg/5ml (2 mg/kg (single) every 24 hours for the first week and (2 mg/kg (single) every 12 hours for the second week, after which NVP is canceled).	It does not comply with the 2016 WHO Guidelines. The infant is given three-component prophylaxis: 3TC + AZT (twice a day) and NVP (once a day) for 2 weeks.	**Page 120:** Infants born to mothers with HIV who are at high risk of acquiring HIV should receive dual prophylaxis with AZT (twice daily) and NVP (once daily) for the first 6 weeks of life, whether they are breastfed or formula-fed.
Order No. 277, page 304: Preventive use of ARVs for the child during breastfeeding: The mother has HIV, she is on ART and plans to breastfeed her baby, and the baby is on **12 weeks** of NVP.	It does not comply with the 2016 WHO Guidelines. These recommendations should be revised in the national protocol.	**Page 120:** Infants of mothers who are receiving ART and are breastfeeding should receive **6 weeks** of infant prophylaxis with daily NVP.
Order No. 277, page 304: HIV infection in the mother, the baby was breastfed, and then switched to formula feeding: ARV prophylaxis is not carried out. Early PCR diagnostics.	It does not comply with the 2016 WHO Guidelines. These recommendations should be revised in the national protocol.	**Page 120:** If infants are receiving replacement feeding, they should be given 4–6 weeks of infant prophylaxis with daily NVP.

Order No. 277, pages 303, 304-306: If formula feeding does not meet the criteria for the AFASS (acceptability, feasibility, availability, stability, and safety of bottle feeding), it is recommended exclusively breastfeeding for 6 months and receiving ART by the mother for the entire breastfeeding period, and the infant taking NVP for 6-12 weeks.	It complies with the 2016 WHO Guidelines.	**Page 120:** Breastfed infants who are at high risk of acquiring HIV, and including those first identified as exposed to HIV during the postpartum period, should continue infant prophylaxis for an additional 6 weeks (total of 12 weeks of infant prophylaxis) using either AZT (twice daily) and NVP (once daily) or NVP alone.
RP-3493, the State program for 2018, paragraph 16; RP-3800, the State Program for 2019-2022, paragraph 8 (https://nrm.uz/): Uninterrupted provision of powder milk formula for children younger than 6 months born to HIV-infected mothers. Purchase and distribution of powder milk formulas at the expense of the State budget.	It complies with the 2016 WHO Guidelines.	**Page 125:** National or subnational health authorities should decide whether health services will principally counsel and support mothers known to be HIV infected to either breastfeed and receive ARV interventions or avoid all breastfeeding.
Monitoring before and after starting ART		
Order No. 336, page 40: **Mandatory tests:** Screening double HIV testing of adults by ELISA, then confirmation by immunoblotting.	It does not comply with the 2016 WHO Guidelines. These recommendations should be revised in the national protocol.	**Page 128:** **Establishing a diagnosis of HIV infection.** HIV testing (serology for adults...)
Order No. 277, page 303: **Mandatory tests:** ELISA is carried out at the age of 18 months to detect seroconversion, confirmation of the diagnosis by immune blotting.	It complies with the 2016 WHO Guidelines.	**Page 128:** **Establishing a diagnosis of HIV infection.** HIV testing (serology for ...children 18 months or older...).
Order No. 277, page 303: **Mandatory tests:** The first HIV DNA PCR test should be performed in the child at the age of 6-8 weeks, and the second test in an infant should be performed at the age of 12 weeks.	It complies with the 2016 WHO Guidelines.	**Page 128:** **Establishing a diagnosis of HIV infection.** (...EID for children younger than 18 months).
Order No. 277, p. 20: **Mandatory tests:** · Determination of the absolute number and percentage of CD4+ - lymphocytes in the blood; · Chest x-ray or computed thermogram; · Serological analysis for HBV (HBsAg); · Serologic testing for HCV.	It complies with the 2016 WHO Guidelines.	**Page 128:** **Establishing a diagnosis of HIV infection.** CD4 cell count TB symptom screening
Order No. 277, page 20: **Research according to indications:** · Serological testing for syphilis. · Swab for gonorrhea and Chlamydia trachomatis (depending on the indication from the vagina, penis, or anus). · Determination of the titer of cryptococcal antigen in patients with CD4 <100/mm3 and symptoms of cryptococcosis. · Determination of CMV antigen (IgM) in patients with CD4 <100/mm3. · Cytological examination of a smear from the cervix. · According to indications, ultrasound (MRI, CT) of the abdominal organs, small pelvis, kidneys, etc. · Examination by an ophthalmologist (preferably repeated every 6 months if the CD4 cell count is <100/mm3 to detect CMV retinitis). · Examination by a gynecologist, including a cytological examination of a cervical smear (PAP-smear), every 6 months (to detect cervical cancer caused by HPV).	It complies with the 2016 WHO Guidelines. Serological testing for HBV/HCV belongs to mandatory testing.	**Page 128:** **Desirable (if feasible):** · HBV (HBsAg) serology · HCV serology · Cryptococcus antigen if CD4 cell count ≤100 cells/mm3 · Screening for STIs · Pregnancy test to assess if ART initiation should be prioritized to prevent HIV transmission to the child · Assessment for major noncommunicable chronic diseases and comorbidities

Order No. 277, page 21: **Routine examination:** Determination of the number of CD4 lymphocytes in the blood every 6-12 months and according to clinical indications.	It complies with the 2016 WHO Guidelines.	**Page 128:** **Follow-up examination before ART is recommended:** CD4 cell count (every 6–12 months in circumstances where ART initiation is delayed)**.**
Order No. 277, page 51: **Before starting ART, mandatory:** · Research on VL; · Determination of the number of CD4 lymphocytes; · Complete blood count before starting AZT; · Determination of ALT, SGOT, total bilirubin (direct and indirect fractions), blood glucose, cholesterol, creatinine. · Serum creatinine and estimated glomerular filtration rate (eGFR) before starting TDF.	It complies with the 2016 WHO Guidelines but refers to mandatory research. Blood pressure measurements and pregnancy tests are not listed on the lab test.	**Page 128:** **ART initiation. It is desirable to conduct:** · Haemoglobin test for starting AZT · Pregnancy test · Blood pressure measurement · Serum creatinine and estimated glomerular filtration rate (eGFR) or starting TDF · Alanine aminotransferase for NVP · Baseline CD4 cell count
Order No. 277, page 51: **Receiving ART. Recommended:** · HIV viral load (6 and 12 months after starting ART, then every 12 months). · CD4 cell count (after 6-12 months while patients are on continuous ART, then every 12 months and if clinically indicated).	It complies with the 2016 WHO Guidelines.	**Page 128:** **Receiving ART. Recommended:** · HIV viral load (at 6 months and 12 months after initiating ART and every 12 months thereafter) · CD4 cell count every 6 months until patients are stable on ART.
Order No. 277, page 51: **Recommended:** Serum creatinine and eGFR in TDF treatment.		**Page 128:** **Receiving ART. Desirable (if feasible):** Serum creatinine and eGFR for TDF.
	It does not comply with the 2016 WHO Guidelines. For a pregnancy test in women of childbearing age who are not planning a pregnancy and are receiving DTG treatment. The national protocol does not recommend low-dose EFV treatment regimens.	**Page 128:** **Receiving ART. Desirable (if feasible):** Pregnancy test, especially for women of childbearing age not receiving family planning and on treatment with DTG or low-dose EFV.
	There are no recommendations in the national protocol.	**Page 128:** **Suspected treatment failure. Desirable (if feasible):** HBV (HBsAg) serology (before switching ART regimen if this testing was not done or if the result was negative at baseline and the patient was not vaccinated thereafter).
Recommendations for switching to second-line ART regimens, including for special patient groups.		
Order No. 277, page 48: **Recommendations for the diagnosis of treatment failure.** Viral load is used as a monitoring tool to detect and confirm the failure of ART. Viral load should be measured 6 and 12 months after starting ART, then every 12 months, or as indicated, to detect treatment failure.	It complies with the 2016 WHO Guidelines.	**Page 129:** **Monitoring the response to ART and diagnosis of treatment failure.** Recommendations for routine monitoring: Routine viral load monitoring can be carried out at 6 months, at 12 months and then every 12 months thereafter if the patient is stable on ART to synchronize with routine monitoring and evaluation reporting.

Order No. 277, page 20: **Mandatory test:** Determination of the absolute number and percentage of CD4 lymphocytes in the blood every 6 and 12 months and according to clinical indications.	Does not comply with WHO 2016 recommendations. These recommendations should be revised in the national protocol. This would allow more rational use of financial costs for more relevant and necessary tests.	**Page 129:** In settings where routine viral load monitoring is available, CD4 cell count monitoring can be stopped in individuals who are stable on ART and virally suppressed.
Order No. 277, page 48: It is recommended that the viral load be used as the preferred monitoring method to identify and confirm treatment failure.	It complies with the 2016 WHO Guidelines.	**Page 129:** Viral load is recommended as the preferred monitoring approach to diagnose and confirm treatment failure.
	These recommendations are not included in the national protocol. Research on VL is regular. There are no interruptions in VL tests in the country. Analyzes are carried out in all AIDS service organizations.	**Page 129:** If viral load is not routinely available, CD4 count and clinical monitoring should be used to diagnose treatment failure.
Order No. 277, page 49: Virologic failure is defined by a persistently detectable viral load exceeding 1000 copies/mL (two consecutive viral load measurements within a 3-month interval with adherence support between measurements) at least 6 months after starting a new ART regimen.	It complies with the 2016 WHO Guidelines.	**Page 129:** Viral failure is defined by a persistently detectable viral load exceeding 1000 copies/ mL (that is, two consecutive viral load measurements within a 3-month interval with adherence support between measurements) after at least 6 months of starting a new ART regimen.
	It is not included in the national protocol.	**Page 129:** Dried blood spot specimens using venous or capillary whole blood can be used to determine the HIV viral load. A threshold of 1000 copies/ mL can be used to determine viral failure when using dried blood spot samples, as defined for testing in plasma.
Order No. 277, page 52: **Clinical failure in adults.** New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition) after 6 months of effective treatment.	It complies with the 2016 WHO Guidelines.	**Page 131:** **Clinical failure in adults.** New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition) after 6 months of effective treatment.
Order No. 277, page 52: **Clinical failure in children.** New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 clinical condition with the exception of TB) after 6 months of effective treatment.	It complies with the 2016 WHO Guidelines.	**Page 131:** **Clinical failure in children.** New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 clinical condition with the exception of TB) after 6 months of effective treatment.
Order No. 277, page 52: **Immunological criteria for treatment failure.** **Adults and adolescents:** CD4 count at or below 250 cells/mm3 following clinical failure or persistent CD4 levels below 100 cells/mm3. **Children younger than 5 years:** persistent CD4 count <200 cells/mm3. **Older than 5 years:** persistent CD4 count <100 cells/mm3 . Without concomitant or recent infection to cause a transient decline in the CD4 cell count.	It complies with the 2016 WHO Guidelines.	**Page 131:** **Immunological criteria for treatment failure.** **Adults and adolescents:** CD4 count at or below 250 cells/mm3 following clinical failure or persistent CD4 levels below 100 cells/mm3. **Children younger than 5 years:** persistent CD4 count <200 cells/mm3. **Older than 5 years:** persistent CD4 count <100 cells/mm3 . Without concomitant or recent infection to cause a transient decline in the CD4 cell count.

Order No. 277, page 52: **Virological failure.** Persistent viral load detection above 1000 copies/mL (two consecutive viral load measurements within 3 months with adherence between measurements) at least 6 months after starting a new ART regimen. **Comments:** An individual must be taking ART for at least 6 months before it can be determined that a regimen has failed.	It complies with the 2016 WHO Guidelines.	**Page 131:** **Virological failure** Viral load above 1000 copies/mL based on two consecutive viral load measurements in 3 months, with adherence support following the first viral load test. **Comment:** An individual must be taking ART for at least 6 months before it can be determined that a regimen has failed.
Order No. 277, page 49: **Immunological response.** CD4 cell count alone is not an indicator of treatment success or failure. On average, during the first year of ART, the CD4 cell count increases by 50-100 cells/mm3. If during the first year of ART the CD4 cell count has not increased by more than 50 cells/mm3, then the immunological failure of the treatment is indicated. Insufficient immunological response may be due to virologic treatment failure, age, and ARV drugs (ZDV). The insufficient immunological response is also possible in the case of late initiation of ART, development of profound immunosuppression, and impaired reparative function of the immune system without the possibility of complete recovery, even with effective ART. This case, with the exclusion of virological failure and other reasons, does not require replacement of ARV drugs or the entire regimen.	It does not comply with the 2016 WHO Guidelines. The national protocol does not recommend assessing ART failure based on CD4.	**Page 131:** **Determining treatment failure in the absence of viral load monitoring.** Where viral load monitoring is not available, clinical monitoring and CD4 monitoring are recommended. However, immunological and clinical criteria have poor sensitivity and specificity to detect treatment failure, particularly at higher CD4 cell counts, and more accurate immunological criteria are yet to be identified, it is important to use CD4 cell counts and clinical assessment to identify those at the highest risk of disease progression and mortality.
Order No. 277, page 57: **Second-line ART regimens for children, adolescents, adults, and pregnant women.** **Adults and adolescents (10 to 18 years old):** **Failed first-line ART regimen:** two NRTIs + EFV (or NVP), 2 NRTIs + DTG. **Preferred second-line regimen :** 2 NRTIs + LPV/r. Alternative second-line regimens: 2 NRTIs + ATV/r or DRV/r.	It complies with the 2016 WHO Guidelines. The national protocol proposes ATV/r is an alternative treatment regimen.	**Page 150:** **What ART regimen to switch to (second-line ART).** **Adults and adolescents:** **Failed first-line regimen:** 2 NRTIs + EFV (or NVP), 2 NRTIs + DTG. **Preferred second-line regimen:** 2 NRTIs + ATV/r or LPV/r. Alternative second-line regimens: 2 NRTIs + DRV/r.
Order No. 277, page 57: **Pregnant or breastfeeding women:** **Failed second-line regimen:** 2 NRTIs + EFV (or NVP). **Preferred second-line regimen:** 2 NRTIs + LPV/r. **Alternative second-line regimens:** 2 NRTIs + ATV/r or DRV/r.	It complies with the 2016 WHO Guidelines. The national protocol proposes ATV/r is an alternative treatment regimen.	**Page 150:** **Pregnant or breastfeeding women:** **Failed second-line regimen:** 2 NRTIs + EFV (or NVP). **Preferred second-line regimen:** 2 NRTIs + ATV/r or LPV/r. **Alternative second-line regimens:** 2 NRTIs + DRV/r.
Order No. 277, page 57: **Children less than 3 years:** **Failed second-line regimen:** 2 NRTIs + LPV/r, 2 NRTIs + NVP. **Preferred second-line regimen:** Continue the ineffective LPV/r regimen and switch to 2 NRTIs + EFV at age 3. **Alternative second-line regimens:** 2 NRTI + RAL.	The national protocol recommends continuing on an ineffective regimen for up to 3 years. The national protocol proposes RAL as an alternative. There is no recommendation to continue the ineffective LPV/r regimen. There is also no mention of switching to a 2 NRTI + EFV regimen at the age of 3 years.	**Page 150:** **Children less than 3 years:** **Failed second-line regimen:** 2 NRTIs + LPV/r, 2 NRTIs + NVP. **Preferred second-line regimen:** 2 NRTIs + RAL, 2 NRTIs + LPV/r. **Alternative second-line regimens:** Maintain the failing LPV/r-based regimen and switch to 2 NRTIsb + EFV at 3 years of age.

Order No. 277, page 57: **Children from 3 years to less than 10 years:** **Failed second-line regimen:** 2 NRTIs + LPV/r, 2 NRTIs + EFV (or NVP). **Preferred second-line regimen:** 2 NRTIs + EFV, 2 NRTIs + LPV/r. **Alternative second-line regimens:** 2 NRTI + RAL, 2 NRTI + ATV/r.	There is no alternative 2 NRTI + RAL regimen in the national protocol.	**Page 150:** **Children from 3 years to less than 10 years:** **Failed second-line regimen:** 2 NRTIs + LPV/r, 2 NRTIs + EFV (or NVP). **Preferred second-line regimen:** 2 NRTIs + EFV, 2 NRTIs + LPV/r. **Alternative second-line regimens:** 2 NRTI + RAL, 2 NRTI + ATV/r.
Order No. 277, page 55: **Preferred second-line ARV regimens for adults:** If AZT was part of the first-line ART, use TDF + 3TC (or FTC) + LPV/r. If TDF was included in the first-line ART, use AZT + 3TC + LPV/r.	There is no preferred ATV r in the national protocol.	**Page 151:** **Summary of preferred second-line ART regimens for adults and adolescents:** If d4T or AZT was used in first-line ART, use TDF + 3TC (or FTC) + ATV/r or LPV/r. If TDF was used in first-line ART, use AZT + 3TC + ATV/r or LPV/r.
Order No. 277, page 55: **Pregnant or breastfeeding women:** **Preferred second-line regimen:** If AZT was included in first-line ART, use TDF + 3TC (or FTC) + LPV/r. If TDF was included in the first-line ART, use AZT + 3TC + LPV/r.	It complies with the 2016 WHO Guidelines.	**Page 151:** **Pregnant or breastfeeding women:** Preferred second-line regimen: Same regimens as recommended for adults and adolescents.
HIV and TB coinfection: **Preferred second-line regimen:** If rifabutin is available, use standard PI-containing regimens as recommended for adults and adolescents. If rifabutin is not available, use the same NRTI backbones as recommended for adults and adolescents plus double-dose LPV/r (that is, LPV/r 800 mg/200 mg twice daily).	It complies with the 2016 WHO Guidelines.	**HIV and TB coinfection:** **Preferred second-line regimen:** If rifabutin is available, use standard PI-containing regimens as recommended for adults and adolescents. If rifabutin is not available, use the same NRTI backbones as recommended for adults and adolescents plus double-dose LPV/r (that is, LPV/r 800 mg/200 mg twice daily).
HIV and HBV coinfection: **Preferred second-line regimen:** AZT + TDF + 3TC (or FTC) + (ATV/r or LPV/r).	It complies with the 2016 WHO Guidelines.	**HIV and HBV coinfection:** **Preferred second-line regimen:** AZT + TDF + 3TC (or FTC) + (ATV/r or LPV/r).
Order No. 277, page 55: · The combination of boosted PI + 2NRTIs is recommended as the preferred second-line ART strategy for adults. · After failure on a ABC + 3TC-based first-line regimen, AZT + 3TC or TDF + 3TC (or FTC) should be used as 2 NRTIs backbone in second-line regimens. · After failure on an AZT + 3TC-based first-line regimen, TDF + 3TC (or FTC) should be used as 2 NRTIs backbone in second-line regimens. · After failure on a TDF + 3TC (or FTC)-based first-line regimen, AZT + 3TC should be used as 2 NRTIs backbone in second-line regimens. · It is recommended to use a fixed-dose combination of two NRTIs as the preferred approach. · ABC for second-line ART is acceptable as a back-up option in special circumstances, but it is not recommended as a preferred option as it does not have a particular advantage over the virological activity of ZDV and TDF against HIV.	It complies with the 2016 WHO Guidelines. d4T and ddI have not been purchased locally or used in treatment regimens since 2013.	**Page 152:** · Second-line ART in adults should consist of two nucleoside reverse-transcriptase inhibitors (NRTIs) plus a ritonavir-boosted protease inhibitor (PI). · The following sequence of second-line NRTI options is recommended: – After failure on a TDF + 3TC (or FTC)-based first-line regimen, use AZT + 3TC as the NRTI backbone in second-line regimens. – After failure on an AZT or d4T + 3TC-based first-line regimen, use TDF + 3TC (or FTC) as the NRTI backbone in second-line regimens. · Use of NRTI backbones as a fixed-dose combination is recommended as the preferred approach · ABC and didanosine (ddI) can be used as NRTI back-up options but add complexity and cost without clinical advantages.

Order No. 277, pages 54-55: The combination of boosted PI + 2 NRTIs is recommended to use as the preferred second-line ART strategy for adults: TDF + 3TC (or FTC) + LPV/r. If TDF is included in the first-line ART, use AZT + 3TC + LPV/r.	It complies with the 2016 WHO Guidelines. The national protocol does not recommend the use of RAL + LPV/r as an alternative option of second-line ART, and there are no recommendations for the use of ATV/r in second-line therapy.	**Page 152:** · Heat-stable fixed-dose combinations of ATV/r and LPV/r are the preferred boosted PI options for second-line ART · Heat-stable fixed-dose combinations of DRV/r can be used as an alternative boosted PI option for second-line ART. · A combination of RAL plus LPV/r can be used as an alterna¬tive second-line ART regimen (conditional recommendation, low-quality evidence).
Order No. 277, page 57: **Second-line ART in children:** Continue ineffective LPV/r-based regimen and switch to 2 NRTIs + EFV at the age of 3; alternative regimen is 2 NRTIs + RAL.	It complies with the 2016 WHO Guidelines.	**Page 156:** Second-line ART for children: After the failure of a first-line LPV/r-based regimen, children younger than 3 years should be switched to a RAL-based second-line regimen.
Order No. 277, page 57: After the failure of a first-line LPV/r-based regimen in children older than 3 years, switch to a second-line regimen containing an NNRTI plus two NRTIs; the preferred NNRTI is EFV: 2 NRTIs + EFV, 2 NRTIs + RAL.	It complies with the 2016 WHO Guidelines.	**Page 156:** After the failure of a first-line LPV/r-based regimen, children older than 3 years should be switched to a second-line regimen containing two NRTIs plus EFV or RAL.
Order No. 277, page 56: After the failure of a first-line NNRTI-based regimen, a boosted PI + 2NRTIs is used for second-line ART; the preferred boosted PI is LPV/r. **Page 57:** ATV/ r can be used as an alternative to LPV/r in children older than 3 months.	It complies with the 2016 WHO Guidelines.	**Page 156:** After the failure of a first-line NNRTI-based regimen, children should be switched to a boosted PI-based regimen. LPV/r or ATV/r are preferred.
Recommendations for the third-line ARVs		
Order No. 277, page 58: Summary of sequencing options for first-, second- and third-line ART regimens in adults, adolescents, pregnant women and children. **Adults and adolescents (> 10 years):** **1st-line regimen:** 2 NRTI + EFV; 2 NRTI + DTG **2nd -line regimen:** 2 NRTI + LPV/r; 2 NRTI + ATV/r or DPV/r **3-line regimen:** DRV/r + DTG (or RAL) ± 1–2 NRTI; DRV/r + 2 NRTI ± NNRTI (ETV)	It complies with the 2016 WHO Guidelines. Genotyping is not carried out in the country.	**Page 161:** Summary of sequencing options for first-, second- and third-line ART regimens in adults, adolescents, pregnant women and children. **Adults and adolescents (> 10 years):** **1st-line regimen:** 2 NRTI + EFV; 2 NRTI + DTG **2nd -line regimen:** 2 NRTI + ATV/r or LPV/r; 2 NRTI + DPV/r **3-line regimen:** DRV/r + DTG (or RAL) ± 1–2 NRTI; DRV/r + 2 NRTI ± NNRTI; Optimize regimen using genotype profile
Page 58: **Pregnant or breastfeeding women:** **1st-line regimen:** 2 NRTI + EFV **2nd -line regimen:** 2 NRTI + ATV/r or LPV/r **3-line regimen:** DRV/r + DTG (or RAL) ± 1–2 NRTI	The national protocol does not include a 2 NRTI + DRV/r regimen as the recommended second-line therapy in pregnant women.	**Page 161:** **Pregnant or breastfeeding women:** **1st-line regimen:** 2 NRTI + EFV **2nd -line regimen:** 2 NRTI + ATV/r or LPV/r; 2 NRTI + DPV/r **3-line regimen:** DRV/r + DTG (or RAL) ± 1–2 NRTI

Children (0-10 years): **1st-line regimen**: 2 NRTI+ LPV/r; 2 NRTI + EFV **2nd -line regimen (children less than 3 years)**: 2 NRTI + RAL **2nd -line regimen (children older than 3 years)**: 2 NRTI + EFV or RAL; 2 NRTI + ATV/r or LPV/r **3-line regimen**: RAL + 2 NRTI; DRV/r + 2 NRTI; DRV/r + RAL ± 1–2 NRTI	The national protocol does not specify DTG as third-line regimens in children aged 0 to 10 years.	**Children (0-10 years):** **1st-line regimen**: 2 NRTI+ LPV/r; 2 NRTI + EFV **2nd -line regimen (If less than 3 years)**: 2 NRTI + RAL **2nd -line regimen (If older than 3 years)**: 2 NRTI + EFV or RAL; 2 NRTI + ATV/r or LPV/r **3-line regimen**: RAL (or DTG) + 2 NRTI; DRV/r + 2 NRTI; DRV/r + RAL (or DTG) ± 1–2 NRTI
Page 57: Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as INSTIs and second-generation NNRTIs and PIs.	It complies with the 2016 WHO Guidelines.	**Page 159:** **Third-line ART. Recommendations:** Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as INSTIs and second-generation NNRTIs and PIs.
Page 58: Adult patients with second-line therapy failure for whom new ARVs are not available should continue with a tolerated regimen. Also, children whose second-line therapy failure for whom new ARVs are not available should continue the regimen with good tolerance.	It complies with the 2016 WHO Guidelines.	**Page 159:** Patients on a failing second-line regimen with no new ARV drug options should continue with a tolerated regimen.
Barriers to access to key drugs recommended by WHO, if available (e.g., lack of registration, not on the list of essential drugs or on procurement lists, high price, etc.)		N/A
Other, not specified above		
Part 5. Prevention and treatment of concomitant infections and diseases		
Recommendations for the prevention and treatment of co-infections, primarily (but not limited to): HIV/viral hepatitis C (HCV), HIV/HBV, HIV/TB		
Page 161: **Criteria to initiate and discontinue co-trimoxazole prophylaxis. Adults with HIV (including pregnant women).** This is prescribed to everyone with advanced HIV infection (clinical stage 3 or 4 or CD4 count ≤350 cells/mm3). In settings with a high prevalence of severe bacterial infections: it should be continued. May be discontinued in clinically stable patients with signs of immunosuppression and/or viral suppression on ART.	It complies with the 2016 WHO Guidelines.	**Page 193:** **Co-trimoxazole prophylaxis for adults.** Co-trimoxazole (CTX) prophylaxis is recommended for adults (including pregnant women) with severe or advanced HIV clinical disease (WHO stage 3 or 4) and/or with a CD4 count ≤350 cells/mm3. In settings where malaria and/or severe bacterial infections (SBIs) are highly prevalent, co-trimoxazole prophylaxis should be initiated regardless of CD4 cell count or WHO stage. Co-trimoxazole prophylaxis may be discontinued in adults (including pregnant women) with HIV who are clinically stable on ART, with evidence of immune recovery and viral suppression.
Page 161: People living with HIV and TB are prescribed with active TB disease, regardless of CD4 count.	It complies with the 2016 WHO Guidelines.	**Page 193:** Routine co-trimoxazole prophylaxis should be given to all HIV-infected patients with active TB disease regardless of CD4 cell count.

Page 161: Children and adolescents with HIV are prescribed, regardless of WHO clinical stage and the number of CD4 cells. Prescribe primarily: (1) everyone younger than 5 years, regardless of WHO clinical stage or CD4 count; (2) everyone older than 5 years with advanced HIV infection (WHO clinical stage 3 or 4) or those with a CD4 count ≤350 cells/mm3.	It complies with the 2016 WHO Guidelines.	**Page 193:** **Co-trimoxazole prophylaxis for HIV-infected infants, children and adolescents.** Co-trimoxazole prophylaxis is recommended for infants, children and adolescents with HIV, irrespective of clinical and immune conditions. Priority should be given to all children younger than 5 years old regardless of CD4 cell count or clinical stage, and children with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and/or those with a CD4 count ≤350 cells/mm3.
Page 161: In settings with low prevalence for severe bacterial infections, prophylaxis may be discontinued for those older than 5 years, clinically stable, with signs of immunosuppression and/or viral suppression on ART.	It complies with the 2016 WHO Guidelines.	In settings with low prevalence for both malaria and bacterial infections, co-trimoxazole prophylaxis may be discontinued for children five years of age and older who are clinically stable and/or virally suppressed on ART for at least six months and with a CD4 count > 350mm3.
Page 161: **HIV-exposed uninfected infants.** It is prescribed to everyone from 4-6 weeks of age until the risk of HIV transmission is eliminated or the likelihood of HIV infection is excluded.	It complies with the 2016 WHO Guidelines.	**Page 193:** **Co-trimoxazole prophylaxis is recommended for HIV-exposed infants** 4 to 6 weeks of age and should be continued until HIV infection has been excluded by an age-appropriate HIV test to establish final diagnosis after complete cessation of breastfeeding.
Page 119: As an initial diagnostic test, GenXpert MTB/RIF should be performed - culture isolation in purulent discharge from fistulas and materials obtained by aspiration or tissue biopsy. **Page 116:** According to the algorithm for diagnosing TB in PLHIV, a bacterioscopic examination of sputum is carried out to detect M. tuberculosis. **Page 120:** Every patient with a presumptive diagnosis of drug-resistant TB should use the GenXpert MTB/RIF test system to determine the resistance of the pathogen to anti-tuberculosis drugs. If rifampicin resistance is identified with GenXpert MTB/RIF, susceptibility testing should be performed to all first- and second-line anti-TB drugs to optimize the use of second-line drugs.	The national protocol states that microscopic examination is mandatory. However, it is recommended for all patients with suspicion using the GenXpert MTB/RIF test system to determine the resistance of the pathogen to anti-TB drugs.	**Page 197:** **TB diagnosis and treatment.** Xpert MTB/RIF should be used rather than conventional microscopy, culture and drug susceptibility testing (DST) as the initial diagnostic test in adults and children suspected of having multidrug-resistant TB (MDR-TB) or HIV-associated TB. Xpert MTB/RIF should be used in preference to conventional microscopy and culture as the initial diagnostic test for cerebrospinal fluid specimens from patients suspected of having TB meningitis. Xpert MTB/RIF may be used as a replacement test for usual practice (including conventional microscopy, culture or histopathology) for testing specific non-respiratory specimens (lymph nodes and other tissues) from patients suspected of having extrapulmonary TB.
	The national protocol does not recommend the use of the LF-LAM test method.	**Page 197:** **LF-LAM** may be used to assist in the diagnosis of active TB in adult inpatients living with HIV, with signs and symptoms of TB (pulmonary and/or extrapulmonary), who have a CD4 count less than or equal to 100 cells/mm3, or people living with HIV who are seriously ill, regardless of CD4 cell count or with unknown CD4 cell count.

Page 130: Indications for preventive treatment. Adults living with HIV, regardless of the degree of their immunodeficiency, including those receiving ART, receive isoniazid prophylaxis at a dose of 300 mg per day for 6 months. The course of isoniazid prophylaxis for PLHIV adults is repeated every 36 months. Prophylactic anti-TB treatment should be started in all PLHIV adults who have been excluded from the diagnosis of active TB, as well as in all HIV-infected children who have clinical or immunological indications for starting ART. PLHIV should receive treatment for LTBI, regardless of test results for latent infection. In addition, they had close contact with patients with infectious forms of pulmonary TB; children older than 12 months living with HIV who have excluded active TB and who have not had contact with TB; children younger than 12 months who have been in contact with a TB patient and have been tested for TB (using special methods), if the examination does not reveal signs of TB infection. The CD4 count is not recommended as a criterion for initiating prophylactic anti-TB therapy. A history of TB disease, pregnancy, or ART are not contraindications for initiating TB preventive treatment.	It complies with the 2016 WHO Guidelines.	**Page 201:** **Isoniazid preventive therapy (IPT).** Adults and adolescents living with HIV should be screened with a clinical algorithm; those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT. Adults and adolescents living with HIV who have an unknown or positive tuberculin skin test (TST) status and are unlikely to have active TB should receive at least six months of IPT as part of a comprehensive package of HIV care. IPT should be given to such individuals regardless of the degree of immunosuppression, and also to those on ART, those who have previously been treated for TB and pregnant women. Adults and adolescents living with HIV who have an unknown or positive tuberculin skin test status and among whom active TB disease has been safely ruled out should receive at least 36 months of IPT. IPT should be given to such individuals regardless of whether or not they are receiving ART. IPT should also be given irrespective of the degree of immunosuppression, history of previous TB treatment and pregnancy.
Page 131: **Isoniazid chemoprophylaxis in children.** When a child's HIV status is first established, if active tuberculosis is excluded, such children, regardless of their age, should be prescribed preventive treatment with isoniazid (10 mg/kg per day) for 6 months. Chemoprophylaxis for TB can be done concurrently with ART. Among children with HIV younger than 12 months, only those who have been in contact with a TB patient, if the examination does not show signs of TB infection, should receive 6 months of IPT. All HIV-infected children are subject to repeated chemoprophylaxis in case of TB risk factors (contact with TB patients in the family, registration of primary infection).	It complies with the 2016 WHO Guidelines.	**Page 201:** Isoniazid prophylactic therapy (IPT) in children. Children living with HIV who do not have poor weight gain, fever or current cough are unlikely to have active TB. Children living with HIV who have poor weight gain, fever or current cough or contact history with a TB case may have TB and should be evaluated for TB and other conditions. If the evaluation shows no TB, they should be offered IPT regardless of their age. · Children living with HIV who are more than 12 months of age and who are unlikely to have active TB on symptom-based screening and have no contact with a TB case should receive six months of IPT (10 mg/kg/day) as part of a comprehensive package of HIV prevention and care. · In children living with HIV who are less than 12 months of age, only those who have contact with a TB case and who are evaluated for TB (using investigations) should receive six months of IPT if the evaluation shows no TB disease
	These recommendations are not included in the national protocol. It is necessary to revise these recommendations in the national protocol.	**Page 201:** **Isoniazid prophylactic therapy (IPT) in children.** All children living with HIV, after successful completion of treatment for TB, should receive IPT for an additional six months.
Page 125: **Treatment of resistant forms of TB and HIV.** All PLHIV with MDR-TB should start ART as soon as possible (within the first eight weeks), regardless of their CD4 cell count.	It complies with the 2016 WHO Guidelines.	**Page 203:** **Multidrug-resistant TB and HIV.** Antiretroviral therapy is recommended for all patients with HIV and drug-resistant TB requiring second-line antituberculosis drugs irrespective of CD4 cell count, as early as possible (within the first eight weeks) following initiation of antituberculosis treatment.

Page 140: **Cryptococcal meningitis.** The preferred diagnostic method is a prompt lumbar puncture with measurement of CSF opening pressure and a rapid test for the determination of cryptococcal antigen (CrAg) in CSF or serum.	It complies with the 2016 WHO Guidelines.	**Page 205:** **Diagnosis of cryptococcal disease.** Prompt lumbar puncture with measurement of CSF opening pressure and rapid CSF cryptococcal antigen (CrAg) assay or rapid serum CrAg (either LA or LFA) is the preferred diagnostic approach).
Page 143: **Primary prevention of cryptococcal infection.** Routine antifungal primary prophylaxis of cryptococcosis in HIV-infected people with CD4 cell counts less than 100 cells/mm³ and a negative CrAg test or unknown CrAg status is not recommended prior to ART initiation unless initiation of ART is likely to be delayed for a long time. Routine serum or plasma CrAg screening prior to ART initiation is necessary followed by pre-emptive antifungal therapy in CrAg-positive patients to reduce the development of cryptococcal disease in patients with CD4 cell counts below 100 cells/mm3.	It complies with the 2016 WHO Guidelines.	**Page 205.** **Prevention of cryptococcal disease.** The routine use of antifungal primary prophylaxis for cryptococcal disease in HIV-infected adults, adolescents and children with a CD4 count less than 100 cells/mm3 and who are CrAg negative or where CrAg status is unknown is not recommended prior to ART initiation unless a prolonged delay in ART initiation is likely. The use of routine serum or plasma CrAg screening in ART-naive adults, followed by pre-emptive antifungal therapy if CrAg positive to reduce the development of the cryptococcal disease, may be considered prior to ART initiation in: **a.** patients with a CD4 count less than 100 cells/mm3; and **b.** where this population also has a high prevalence (>3%) of cryptococcal antigenaemia.
Page 141: **Induction therapy (≥2 weeks):** **a.** Liposomal amphotericin B + flucytosine; **b.** Amphotericin B deoxycholate + flucytosine; **c.** Amphotericin B deoxycholate + fluconazole.	There is no alternative treatment regimen in the national protocol.	**Page 206:** **Induction, consolidation and maintenance antifungal treatment regimens:** **a.** Amphotericin B + flucytosine; **b.** Amphotericin B + fluconazole; **c.** Amphotericin B short course (5–7 days) + high-dose fluconazole (to complete 2 weeks of induction); **d.** Fluconazole high dose + flucytosine, when amphotericin B is not available; **e.** Fluconazole high dose alone, when amphotericin B is not available.
Page 141: **Consolidation therapy (8 weeks):** Fluconazole 1 x 400 mg/day orally (loading dose 1 x 800 mg on the first day).	It complies with the 2016 WHO Guidelines.	**Page 206:** **As a consolidation phase of treatment:** Fluconazole 400-800 mg per day.
Page 142: **Preventive therapy:** Fluconazole 800 mg/day (or 12 mg/kg per day if the patient is younger than 19 years) orally for 2 weeks, then 400 mg/day (or 6 mg/kg per day up to 400-800 mg/day if the patient is younger than 19 years) orally for 8 weeks and continuous maintenance treatment with fluconazole at a dose of 200 mg/day.	It complies with the 2016 WHO Guidelines.	**Page 206:** **As a maintenance treatment:** fluconazole 200 mg daily (6 mg/kg/day up to 200 mg/day if below 19 years). For localized non-meningeal disease, or in patients with isolated serum CrAg positivity. Fluconazole 800 mg/day (or 12 mg/kg/day if below 19 years) for two weeks, then 400 mg/day (or 6 mg/kg/day up to 400–800 mg/day if below 19 years) for eight weeks, and continued maintenance with fluconazole 200 mg/day is recommended.

Page 142: **Prevention, monitoring and treatment of the toxic effects of amphotericin B:** In HIV-infected adults receiving amphotericin B–containing regimens for treatment of cryptococcal disease, a minimum package of toxicity prevention, monitoring and management is recommended to minimize the serious amphotericin B–related toxicities (hypokalaemia and nephrotoxicity).	It complies with the 2016 WHO Guidelines.	**Page 207:** **Prevention, monitoring and treatment of amphotericin B toxicity:** In HIV-infected adults receiving amphotericin B–containing regimens for treatment of cryptococcal disease, a minimum package of toxicity prevention, monitoring and management is recommended to minimize the serious amphotericin B–related toxicities of hypokalaemia and nephrotoxicity.
Page 142: In HIV-infected patients with cryptococcal meningitis, it is not recommended to start ART immediately, due to the high risk of immune reconstitution inflammatory syndrome (IRIS), which may be life threatening. If cryptococcal meningitis is diagnosed, ART initiation should be postponed there is evidence of a sustained clinical response to antifungal therapy, and after 4 weeks of induction and consolidation treatment with amphotericin B in combination with flucytosine or fluconazole, or after 4-6 weeks of treatment with a high-dose oral fluconazole induction and consolidation regimen.	It complies with the 2016 WHO Guidelines.	**Page 207:** **Timing of ART initiation.** Immediate ART initiation is not recommended in HIV-infected patients with cryptococcal meningitis due to the high risk of IRIS that may be life-threatening. In HIV-infected adults, adolescents and children with a recent diagnosis of cryptococcal meningitis, ART initiation should be deferred until there is evidence of a sustained clinical response to antifungal therapy, and after 4 weeks of induction and consolidation treatment with amphotericin B–containing regimens combined with flucytosine or fluconazole, or after 4–6 weeks of treatment with a high-dose oral fluconazole induction and consolidation regimen.
Page 142: **Discontinuation of azole maintenance treatment (secondary prophylaxis).** **I**n HIV-infected adults and adolescents with the successfully treated cryptococcal disease (meningeal and non-meningeal), discontinuation of antifungal maintenance treatment is recommended based on the following criteria: **a**. If HIV viral load monitoring is not available; when patients are stable and adherent to ART and antifungal maintenance therapy for at least one year and **b.** If HIV viral load monitoring is available; patients are stable and adherent to ART and antifungal maintenance treatment for at least one year and with CD4 count greater than or equal to 100 cells/mm3 (two measurements six months apart) and a suppressed viral load. (conditional recommendation, low-quality evidence). In HIV-infected children aged between 2 and 5 years with successfully treated cryptococcal disease (meningeal and non-meningeal), discontinuation of antifungal treatment maintenance is recommended if the child is stable and adherent to ART and antifungal maintenance treatment for at least one year and with a CD4 cell count percentage greater than 25% or absolute count greater than 750 cells/mm3 (two measurements six months apart). Maintenance therapy for cryptococcal disease should NOT be discontinued in children less than two years. Maintenance treatment for cryptococcal disease should be restarted if CD4 count drops to 100 cells/mm3 or below in HIV-infected adults and adolescents (or CD4 cell count less than or equal to 25% or 750 cells/mm3 in children aged between two and five years), or if a WHO stage 4 clinical event occurs, irrespective of patient age.	It complies with the 2016 WHO Guidelines.	**Page 207:** **Discontinuation of azole maintenance treatment (secondary prophylaxis)** In HIV-infected adults and adolescents with the successfully treated cryptococcal disease (meningeal and non-meningeal), discontinuation of antifungal maintenance treatment is recommended based on the following criteria: **a**. If HIV viral load monitoring is not available; when patients are stable and adherent to ART and antifungal maintenance therapy for at least one year and **b.** If HIV viral load monitoring is available; patients are stable and adherent to ART and antifungal maintenance treatment for at least one year and with CD4 count greater than or equal to 100 cells/mm3 (two measurements six months apart) and a suppressed viral load. (conditional recommendation, low-quality evidence). In HIV-infected children aged between 2 and 5 years with successfully treated cryptococcal disease (meningeal and non-meningeal), discontinuation of antifungal treatment maintenance is recommended if the child is stable and adherent to ART and antifungal maintenance treatment for at least one year and with a CD4 cell count percentage greater than 25% or an absolute count greater than 750 cells/mm3 (two measurements six months apart). Maintenance therapy for cryptococcal disease should NOT be discontinued in children less than two years. Maintenance treatment for cryptococcal disease should be restarted if CD4 count drops to 100 cells/mm3 or below in HIV-infected adults and adolescents (or CD4 cell count less than or equal to 25% or 750 cells/mm3 in children aged between two and five years), or if a WHO stage 4 clinical event occurs, irrespective of patient age.

Page 247: **Management of patients with HBV/HIV co-infection.** ART is recommended, regardless of the presence or absence of an indication for hepatitis B treatment, if the CD4 cell count is less than 500 cells/mm3.	It does not comply the 2016 WHO Guidelines. These recommendations should be revised in the national protocol.	**Page 208:** **Viral hepatitis B and C.** Treatment should be given to all people living with HIV regardless of CD4 count.
Page 244: **Management of patients with HBV/HIV co-infection.** Who is prescribed therapy? All patients with chronic hepatitis B, detectable HBV DNA ≥ 2000 IU/mL, ALT> above normal or normal, and/or fibrosis should be treated. Patients with compensated or decompensated cirrhosis require treatment with any HBV DNA level and regardless of ALT level.	It complies with the 2016 WHO Guidelines.	**Page 208:** Nevertheless, in settings where prioritization is required, people coinfected with HIV and HBV and evidence of severe chronic liver disease should be considered a priority for ART. WHO recommends that adults, adolescents and children with chronic hepatitis B and clinical evidence of cirrhosis (or cirrhosis based on the non-invasive APRI test score >2 in adults) should be treated regardless of alanine aminotransferase (ALT) levels, hepatitis B e antigen (HBeAg) status or HBV DNA levels.
Page 250: **Patients with HBV/HIV co-infection and clinical manifestations of liver cirrhosis.** All patients with compensated and decompensated cirrhosis of the liver should be on ART with a regimen that includes TDF, 3TC (or FTC). It is desirable that the ART regimen should include 2 drugs with dual activity - against HBV and HIV. TDF and FTC or 3TC are preferable.	It complies with the 2016 WHO Guidelines.	**Page 208:** **Viral hepatitis B and C.** The recommended NRTI drugs for ART – TDF with 3TC or FTC – are active against HBV.
	It is not included in the national protocol due to financial constraints.	**Page 208.** **Viral hepatitis B and C.** If ARV drugs need to be changed because of HIV drug resistance or toxicity, then TDF with 3TC or FTC should be continued together with the new ARV drugs. The risk of HBV infection may be higher in HIV-infected adults. All people newly diagnosed with HIV should, therefore, be screened for hepatitis B surface antigen (HBsAg) and vaccinated if non-immune.
Page 266: **Patients with HCV/HIV co-infection who need HIV-only treatment.** ART in patients with HCV/HIV co-infection is initiated according to the recommendations for the treatment of patients with HIV mono-infection. If ART is provided, it is necessary to make sure that it is stable and only then start treatment for hepatitis C. ART is continued.	It complies with the 2016 WHO Guidelines.	**Page 209:** **Management of patients with HIV and hepatitis C coinfection with.** In general, clinical stabilization of HIV disease with ART is advisable prior to start treatment for HCV, especially in people with advanced immunosuppression (CD4 count below 200 cells/mm3).
Order of the MoH of RUz, No. 277, dated April 30, 2018, Annex 8, pages 243-252: The National clinical protocol "Viral hepatitis B and HIV infection: tactics of managing patients with coinfection." **Order of the MoH of RUz, No. 277, dated April 30, 2018, Annex 8, Page 277:** The National clinical protocol "Viral hepatitis C and HIV infection: tactics of managing patients with coinfection."	It complies with the 2016 WHO Guidelines.	**Page 208** **Prevention and treatment of viral hepatitis.**
Prevention and treatment of relevant non-communicable diseases: · Cardiovascular diseases; · Depression; · Diseases of the central nervous system; · Kidney disease; · The use of psychoactive substances.		

Pages 18, 21: **Initial physical examination of HIV patients:** · Measurement of blood pressure; · Initial health assessment in patients who are at increased risk of cardiovascular complications while taking ARV drugs or who have an increased risk of endocarditis. **Page 20:** For mandatory instrumental examinations of HIV patients: ECG, the frequency of ECG is once every 12 months.	It complies with the 2016 WHO Guidelines.	**Page 115:** **Assessment and management of cardiovascular disease.** Assessment and management of cardiovascular risk should be provided for all individuals living with HIV according to standard protocols recommended for the general population. Strategies for the prevention and risk reduction of cardiovascular diseases by addressing modifiable factors such as high blood pressure, smoking, obesity, unhealthy diet and lack of physical activity should be applied to all people living with HIV.
Page 355: **Nutritional issues for children with HIV.** HIV infection and malnutrition form a vicious circle of immune system dysfunction, infectious disease and malnutrition, where dietary intake is reduced when nutrient requirements are increased. Inadequate intake of nutrients from food for a long time ultimately leads to malnutrition (dystrophy). In case of dystrophy, there can be both a weight deficit of body (malnutrition, malnutrition) and excess body weight (overeating, obesity). Obesity is a major public health concern as obese individuals are at increased risk of developing cardiovascular disease (CVD). In particular, central obesity, in which body fat accumulates in the trunk, is a recognized risk factor for CVD. Central obesity is one of the clinical manifestations of metabolic syndrome, which includes dyslipidemia. This section provides a brief summary of the essential nutrients found in foods that are necessary for human health.	It complies with the 2016 WHO Guidelines.	**Page 222:** **Nutrition for children living with HIV.** Nutritional assessment is essential to identify malnutrition and growth faltering early. Infants and children should undergo initial nutritional assessment (evaluation of nutritional status, diet and symptoms) and then be weighed and have the height measured at each visit, and monitored with reference to WHO or national growth curves. Growth monitoring should also be integrated into the assessment of ART response. If poor growth is identified, then the further assessment should be performed to determine the cause, and plan an appropriate response.
Page 357: **Introduction to human nutrition.** Solid knowledge of the basic principles of human nutrition is essential for all healthcare workers. Nutritional science includes the study of all processes of growth and development, maintenance of vital functions, and restoration of living systems that need food and the nutrients they contain. In addition, nutritional science includes the study of foods and nutrients. A healthy diet includes many foods that, when combined, contain enough of all nutrients but overnutrition can be harmful to health. **Page 173:** **Cachexia syndrome.** The presence of cachexia syndrome is a reason for talking about proper nutrition. Increasing physical activity and sports may also make sense. Supportive parenteral nutrition only helps in case of malabsorption.	It complies with the 2016 WHO Guidelines.	**Page 221:** **Nutrition for adults and adolescents living with HIV.** Low energy intake combined with increased energy demands due to HIV infection and related infections may lead to HIV-related weight loss and wasting. In addition, altered metabolism, reduced appetite and higher incidence of diarrhoea may lower nutrient intake and absorption and lead to nutrient losses. These effects may all be compounded in low-income and food-insecure contexts. Low body mass in adults (body mass index less than 18.5 kg/m2) and weight loss and wasting in children are all independent risk factors for HIV disease progression and mortality. Nutritional assessment (anthropometry, clinical and dietary assessment), counselling and support should be an integral component of HIV care and conducted at enrolment in care and monitored across the care continuum. Malnourished HIV-infected patients, especially in food-insecure contexts, may require food supplements in addition to ART to support nutritional recovery. Weight loss or failure to regain or maintain a healthy weight at any stage of HIV infection and/or while on ART should trigger further assessment and appropriate interventions.
Pages 203-205: **Tactics for affective disorders. Depression.** Symptoms of depression are listed; treatment and doses are indicated; recommendations are given for consulting a psychiatrist about treatment; recommendations for home care; recommendations for the treatment of patients with mild depressive episodes, moderate depressive episodes, and severe depressive episodes with psychosis are given.	It complies with the 2016 WHO Guidelines.	**Page 219:** **Assessment and management of depression in people living with HIV.** Assessment and management of depression should be included in the package of HIV care services for all individuals living with HIV.

Pages 140-155: **Nervous system infections.** Many bacterial, viral, and fungal OIs can cause CNS damage. The protocol contains the most common CNS damages of an infectious nature (toxoplasmosis, herpetic encephalitis, cytomegalovirus encephalitis, cryptococcal meningitis). Many neurological symptoms and syndromes of the central nervous system and peripheral nervous system, HIV-associated infectious and non-infectious genesis were described.	The 2016 WHO Guidelines do not contain recommendations for CNS diseases.	
Pages 184-197: **HIV infection at the advanced stages.** There are the WHO three-stage regimen of pain therapy, general rules for helping with various symptoms, drug treatment of pain and its basic rules for the treatment of pain syndrome, drug treatment of nausea and vomiting, where the use of psychoactive drugs is described in the treatment regimens.	Patient management tactics comply with the 2006 WHO Guidelines, but there is no specification for PWID.	**Page 221:** **Drug use and drug use disorders.** Experts from WHO, UNODC and UNAIDS recommend a comprehensive package of nine interventions for HIV prevention, treatment and care for people who inject drugs.
Order of the MoH of RUz, No. 336, dated May 24, 2018, pages 127-131: Support and quality control of syringe and needle exchange.	It complies with the 2016 WHO Guidelines.	**Page 30:** **Recommendations. Key populations.** Community-based HIV testing services for key populations linked to prevention, treatment and care services are recommended, in addition to routine facility-based HIV testing services, in all settings.
Part 6. Health service provision		
Provision of health care services, including, but not limited to: · Recommendations for the decentralization of services, · Recommendations for redistribution and delegation of services, · Recommendations for service integration.		
Order No. 336, page 89: Health care for HIV-infected patients is provided by trained HIV specialists in public healthcare facilities. Routine medical monitoring of HIV-infected patients is carried out by general practitioners of primary healthcare facilities and an infectious disease physician of the district multidisciplinary clinic. HIV-infected patients receive inpatient treatment in regional healthcare facilities, national/ regional clinics, regional infectious diseases hospitals, specialized outpatient and day hospitals. Health care for HIV-infected patients in penitentiary institutions is provided by medical institutions of the Ministry of Internal Affairs based on the methodological recommendations of the AIDS Center. Regional AIDS centers and district outpatient clinics at the place of residence conduct monitoring and treatment of an HIV-infected patient. **Order No. 277, page 111:** An HIV-infected pregnant woman in need of PMTCT receives ARVs in accordance with the national clinical protocol (Annex 1, paragraph 1) in the territorial and district AIDS centers, as well as in healthcare facilities, at the patients' request. ARVs are provided for the woman monthly before delivery. In case of a positive HIV rapid test result, the pregnant woman receives an emergency PMTCT at the obstetric facility. **Order No. 277, page 104:** Based on the approved national and regional plans for the provision of ART, in accordance with the current regulatory documents, the district AIDS center distributes a 6-month supply of drugs, test systems and consumables in regions. Based on the requirements of the district (city) medical association, a monthly supply of ARVs is issued from the warehouse of the territorial AIDS center.	It complies with the 2016 WHO Guidelines.	**Page 243:** Following an HIV diagnosis, a package of support interventions should be offered to ensure timely linkage to care for all people living with HIV (strong recommendation, moderate-quality evidence). The following interventions have demonstrated benefit in improving linkage to care following an HIV diagnosis: · · streamlined interventions to reduce time between diagnosis and engagement in care, including (i) enhanced linkage with case management, (ii) support for HIV disclosure, (iii) patient tracing, (iv) training staff to provide multiple services and (v) streamlined services (moderate-quality evidence); · peer support and navigation approach for linkage (moderate-quality evidence); and · quality improvement approaches using data to improve linkage. **Page 246:** Comprehensive home-based HIV testing, which includes offering home assessment and home-based ART initiation. Intensified post-test counselling by community health workers.

Order No. 277, pages 64-74: Algorithms for diagnostics and issues of managing treatment of STIs are stated; the responsibility rests with specialists of the dermatovenerological service. **Order No. 277, pages 94-101:** For an HIV-infected mother: ensuring adherence and continuation of lifelong ARV therapy, providing access to reproductive health (RH) and STI prevention services, social support. **Order No. 277, pages 303-305:** For the child: the continuation of preventive therapy and timely testing in accordance with the clinical protocol, ensuring safe feeding, disease prevention, social support in full compliance with international HIV policies. **Page 116:** Provision of TB diagnostics services to PLHIV. The National HIV Program, in close cooperation with the National TB Program, should ensure that active forms of TB are detected in PLHIV. Each of the services must provide and ensure a full-fledged opportunity to diagnose both diseases within their healthcare facilities. It is recommended to invite an HIV specialist to participate in the TB/MDR-TB council to discuss each case of MDR-TB/HIV co-infection. Such extended councils should consider the recommended antituberculosis therapy regimens, timing and ART regimens.		**Page 246:** Providing assistance with transport, such as transportation vouchers, if the ART site is far from the HIV testing service site Decentralized ART provision and community-based distribution of ART. **Page 246:** Integrated services, where HIV testing, HIV prevention, treatment and care, TB and sexually transmitted infection (STI) screening and other relevant services are provided together at a single facility or site.
Order No. 277, page 301: Support to women with HIV in the maternity clinic. Emphasis on the inadmissibility of discriminatory treatment of the pregnant woman in a maternity clinic because of HIV. **Order No. 277, pages 95-96:** The National clinical protocol "Support for the reproductive health of people living with HIV." Health care should be comprehensive and patient-oriented, that is, meet the lifelong needs of PLHIV. PLHIV should not be discriminated, regardless of behavior-associated risk factors. The Resolution of the President of the Republic of Uzbekistan of January 25, 2018, No. 3493, approved the National Action Plan, which provides for a wide range of preventive, educational and diagnostic measures for the entire population, including migrants, with the involvement of local governments and the public.		
Order of the MoH of RUz, No. 277, Annex 14 "Organization of care, healthcare, psychological and social support for HIV-infected children," pages 327-344. Medical and psychological aspects of disclosing the HIV diagnosis to a child. HIV-positive status should be disclosed to the child by a person with whom he/she has a close and trusting relationship (preferably parents), at a convenient time and moment in terms of age, child development, life situation, health status, etc. HIV-positive status should be disclosed only when the child has received preliminary relevant information and has successfully assimilated it, which can be checked with special games, tasks, and conversations with the child. While disclosing HIV status to a child, specialists should keep in mind that parents are the most important people for the child, they take care of him/her and are responsible for the child and his/her health. And specialists, in this case, are only intermediaries in the process of disclosing HIV status, and their relationship with the child's parents should be based on the principles of partnership.	It complies with the 2016 WHO Guidelines.	**Page 243:** **Support in disclosing HIV status.**

Order No. 277, page 323: Support and self-help groups for PLHIV (including support groups for adolescents with HIV who know their HIV status). Today, Uzbekistan has a model of work with HIV-infected children based on the model of Day centers for children and families affected by HIV. Such centers were established at the AIDS centers. The main tasks of the Centers are to create conditions for psychological and social adaptation of HIV-positive children, to develop and implement measures for psychological and social support and assistance to children and adolescents with HIV, aimed at their integration into society. The centers, in accordance with their tasks: · provide various types of psychosocial services (psychological, socio-pedagogical, socio-medical, legal and informational) for HIV-positive children and their families; · provide counseling and educational activities (preparing parents, counseling and providing psychological support to families and children before starting ART treatment, counseling on adherence to treatment of parents and children; · organize interest clubs, contests, children's parties; · attract parents or persons acting in their stead to cooperation, providing them with methodological recommendations; · organize the work of self-help/-support groups for HIV-positive adolescents, as well as parents or persons acting in their stead; · cooperate with health care institutions, educational institutions and other organizations that provide assistance to HIV-positive children and adolescents; · refer, if necessary, persons who applied to the Center, to specialized institutions according to their needs. Clients of such centers can be: · HIV positive children; · families and the close environment of HIV-positive children; Order of the MoH of RUz, No. 277, Annex 14 "Organization of care, healthcare, psychological and social support for HIV-infected children," page 383. Psychological and pedagogical support for HIV-infected children in a children's institutional setting.	It complies with the 2016 WHO Guidelines.	**Page 251:** Programs should provide community support for people living with HIV to improve retention in HIV care (strong recommendation, low-quality evidence). The following community-level interventions have demonstrated benefit in improving retention in care: · package of community-based interventions (children: low-quality evidence; adults: very low-quality evidence) · adherence clubs (moderate-quality evidence) · extra care for high-risk people. **Page 274:** · Adolescent-friendly health services should be implemented in HIV services to ensure engagement and improved outcomes **Page 281:** HIV programs should: · provide people-centered care that is focused and organized around the health needs, preferences and expectations of people and communities, upholding individual dignity and respect, especially for vulnerable populations, and engage and support people and families to play an active role in their own care by informed decision-making; · offer safe, acceptable and appropriate clinical and non-clinical services in a timely fashion, aiming to reduce morbidity and mortality associated with HIV infection, and to improve health outcomes and quality of life in general; and · promote efficient and effective use of resources.
	There are no such recommendations in national protocols. The exchange of information is carried out in a paper form. An electronic HIV tracking database is being introduced.	**Page 249** **Laboratory connectivity.** Electronic communication can be considered to transfer test results and reduce delays in acting on the results of early infant diagnosis and other essential laboratory tests.
Order No. 336, page 51: Method for CD4 cell count testing. Methods for assessing the state and nature of immunodeficiency are used to assess the immune status. The method for determining CD4 lymphocytes is carried out at national and regional laboratories.	It complies with the 2016 WHO Guidelines.	**Page 248:** **CD4 cell count testing at the point of care.** CD4 cell count testing at the point of care can be used to prioritize patients for urgent linkage to care and ART initiation.
	There are no recommendations in national protocols due to funding constraints.	**Page 255:** mobile phone text messages cognitive-behavioural therapy behavioural skills training and medication adherence training.

Order No. 277, page 108: ARV drugs for PLHIVs, traveling abroad for a long time, or their authorized representatives are issued for a period not exceeding 3 months, and for 6 months in exceptional cases.	It complies with the 2016 WHO Guidelines.	**Page 259.** Less frequent clinical visits (3–6 months) are recommended for people stable on ART Less frequent medication pickup (3–6 months) is recommended for people stable on ART.
	These recommendations are not included in the national protocol. ART is carried out exclusively by AIDS-service organizations. The current law on HIV infection and other regulations do not allow the implementation of these 2016 WHO Guidelines.	**Page 262:** Trained and supervised lay providers can distribute ART to adults, adolescents and children living with HIV. Trained non-physician clinicians, midwives and nurses can initiate first-line ART (strong recommendation, moderate-quality evidence). Trained non-physician clinicians, midwives and nurses can maintain ART. Trained and supervised community health workers can dispense ART between regular clinical visits.
	There are no recommendations in the regulatory documents of the country. According to regulatory documents, blood sampling is carried out only by health workers.	**Page 265:** Trained and supervised non-laboratory staff, including laypeople, can undertake blood finger-prick for sample collection.
Order No. 277, page 16: Follow-up monitoring of PLHIV is provided by specialists from the AIDS Center and infectious disease specialists (physicians of IDR), general practitioners of healthcare facilities under the methodological guidance of a physician from the AIDS Center. In case of decentralization (transfer of a patient to CHF/DHF to continue ART) and/or referral of a patient for hospitalization (regional infectious diseases hospitals), as well as when transferring a patient to another RC AIDS, an extract from the health record and a referral form are filled out. Health examination should include laboratory tests and counseling to identify and prevent problems associated with HIV infection itself, as well as with other diseases and conditions that may affect the treatment of HIV infection, especially when interacting with ART.	It partially complies with the 2016 WHO Guidelines. The initiation of ART for patients is decentralized at regional levels. Lower district levels of health care (facilities, close to the place of residence of patients) continue therapy.	**Page 266:** Decentralization of HIV treatment and care should be considered as a way to increase access to and improve retention in care: • initiation of ART in hospitals with the maintenance of ART in peripheral health facilities; • initiation and maintenance of ART in peripheral health facilities; and • initiation of ART at peripheral health facilities with maintenance at the community level.
	There are no recommendations in national protocols and other normative documents. OST is not used in the country.	**Page 45:** ART in settings providing opioid substitution therapy. ART should be initiated and maintained in people, relevant to criteria, living with HIV at care settings where opioid substitution therapy (OST) is provided.
	OST is not used in the country.	**Page 270:** ART should be initiated and maintained in people, relevant to criteria, living with HIV at care settings where opioid substitution therapy (OST) is provided.
	There are no recommendations in the regulatory documents.	**Page 269:** In settings with a high burden of HIV and TB, ART should be initiated for people living with HIV in TB treatment settings, with linkage to ongoing HIV care and ART. In settings with a high burden of HIV and TB, TB treatment may be provided for people living with HIV in HIV care settings where a TB diagnosis has also been made
The State program, RP 3493 of 2018, paragraph 15: Providing syndromic treatment of sexually transmitted infections for HIV risk groups. Creation of a working group. Creation of “friendly rooms” within the structure of AIDS centers.	It complies with the 2016 WHO Guidelines.	**Page 271:** Sexually transmitted infection (STI) and family planning services can be integrated within HIV care settings.

The State program for 2019-2022, approved by the Resolution of the Presidential, RP 3800 of 2018, paragraph 11: Providing continuous functioning of 15 “friendly rooms” at 15 regional AIDS centers to conduct preventive measures and syndromic treatment among people with an increased risk to be infected with sexually transmitted infections (STIs) and HIV, providing them with psychological assistance. Provision of necessary medicines and products using the local budget.	It complies with the 2016 WHO Guidelines.	**Page 46:** STI and family planning in HIV care settings. Sexually transmitted infection (STI) and family planning services can be integrated within HIV care settings.
Order of the MoH of RUz, No. 336, dated May 24, 2018, page 130: Distribution of preventive products to clients. The distribution of preventive measures based on analytical data collected in the administrative districts of the republic, based on the needs of clients, is conducted based on the following criteria: · Number of syringes per year per person who injects drugs - from 100 to 400; · Number of alcohol wipes per syringe - 2 pcs.; · Information and educational materials. Interviewing of clients, who applied to the anonymous consulting room for screening for tuberculosis, aims to improve the prevention component among people of vulnerable groups for HIV and TB.	There are no recommendations to use lubricants in the national protocols. OST is not used in the country and there is no normative document.	**Page 23.** Provision of male or female condoms and lubricants and guidance on their use. Provision of or referral to prevention, counselling, support and other services as appropriate, including screening and treatment for tuberculosis (TB) and sexually transmitted infections (STIs), prophylaxis for opportunistic infections, contraception, antenatal care, opioid substitution therapy, and access to sterile needles and syringes.
	There are no recommendations in national regulatory documents. The country's AIDS service and healthcare testing services are just starting decentralization. A government document regarding the decentralization of testing services up to primary health care is currently being developed.	**Page 298:** Tiered laboratory network at various levels of the healthcare delivery system 1. National reference laboratory: · Enzyme immunoassays for diagnosis · Higher throughput CD4 count testing · HIV molecular technologies, including HIV viral load testing and quantitative and qualitative early infant diagnosis · HIV resistance testing 2. Regional or provincial reference laboratory: · Enzyme immunoassays for diagnosis · Higher throughput CD4 count testing · HIV molecular technologies, including HIV viral load testing and quantitative and qualitative early infant diagnosis 3. District-level laboratory: · Enzyme immunoassays for diagnosis · Low-throughput CD4 count testing · Chemistry, haematology and microbiology 4. Primary care setting: · HIV rapid diagnostic tests and other point-of-care tests · Collecting dried blood spots 5. Community-based and community outreach. · HIV rapid diagnostic tests · Collecting finger-prick samples for testing