Approved
by the Joint Commission
on the quality of medical
services of the Ministry of
Health of the Republic of
Kazakhstan
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Protocol No. 180

CLINICAL PROTOCOL FOR THE DIAGNOSIS AND TREATMENT OF HIV INFECTION IN ADULTS

I. INTRODUCTORY PART:

1.1 ICD-10 code(s):

Code	Name
V20-24	**Human immunodeficiency virus** disease
B20.0	Disease caused by HIV, with manifestations of mycobacterial infections (Disease caused by HIV, with manifestations of tuberculosis)
B20.1	Disease caused by HIV, with manifestations of other bacterial Infections
Q20.2	Disease caused by HIV, with manifestations of cytomegalo-viral Disease
B20.3	HIV disease with manifestations of other viral infections
B20.4	HIV-related disease with candidiasis
Q20.5	Disease caused by HIV, with manifestations of other mycoses
B20.6	HIV-related disease with manifestations of pneumonia caused by Pneumocystis carinii
Q20.7	HIV disease with multiple infections
B20.8	Disease caused by HIV, with manifestations of other infectious and parasitic diseases
Q20.9	Disease caused by HIV, with manifestations of unspecified infectious and parasitic diseases
Q21.0	HIV disease with manifestations of Kaposi's sarcoma
B21.1	HIV-related disease with Burkitt's lymphoma
Q21.2	Disease caused by HIV, with manifestations of other non-Hodgkin's Lymphoma
Q21.3	Disease caused by HIV, with manifestations of other malignant neoplasms of lymphatic, hematopoietic and related Tissue

Q21.7	Disease caused by HIV, withmanifestations of multiple malignant neoplasms
Q21.8	Disease caused by HIV, with manifestations of other malignant Neoplasms
Q21.9	Disease caused by HIV, with manifestations of unspecified malignant neoplasms
B22.0	HIV disease with manifestations of encephalopathy
Q22.1	Disease caused by HIV, withmanifestations of lymphatic interstitial pneumonitis
Q22.2	Disease caused by HIV, with manifestations of debilitating syndrome (with manifestations of the extinction of life; sudden weight loss syndrome)
Q22.7	Disease caused by HIV, with manifestations of multiple diseases, classified under other headings
B23.0	Acute HIV-infectious syndrome
Q23.1	Disease caused by HIV, withmanifestations (persistent) generalized lymphadenopathy
Q23.2	Disease caused by HIV, with manifestations of hematological and immunological disorders not classified in others Filed under
B23.8	Disease caused by HIV, with manifestations of other specified States
B24	Disease caused by the human immunodeficiency virus (HIV), unspecified (acquired immunodeficiency syndrome ; AIDS-associated complex)
O98.7	Human immunodeficiency virus [HIV] disease, complicating pregnancy, childbirth and the postpartum period
R75	Laboratory detection of human immunodeficiency virus [HIV] (non-conclusive HIV test detected in children)
Z20.1	Contact with the patient and the possibility of contracting tuberculosis
Z20.6	Contact with the patient and the possibility of infection with the virus human immunodeficiency [HIV]
Z21	Asymptomatic infection status caused by the virus human immunodeficiency [HIV]
Z29.2	Another type of preventive chemotherapy
Z29.8	Other refined preventive measures

1.2 Date of development/revision of **the protocol:** 2017 , 2019 (2022 revision).

1.3 Abbreviations used in the protocol:

3TC Lamivudine

ABC	Abacavir
AZT, ZDV	Zidovudine
ATV	Atazanavir
BIC	Biktegravir
COBI	Cobicistat
.DRV	Darunavir
DRV/c	Darunavir boosted with cobicistat
DRV/r	Darunavir boosted with ritonavir
DTG	Dolutegravir
EFV	Efavirenz
ETV	Etravirine
ELV	Elvitegravir
FTC	Emtricitabine
HBcAg	Hepatitis B virus nuclear antigen
HBsAg	Hepatitis B virus surface antigen
HLAB*5701	Allele 5701 of locus B of the main complex Human histocompatibility
IgG	Immunoglobulin G
IgM	Immunoglobulin M
LPV/r	Lopinavir boosted with ritonavir
MTB/RIF	Rapid molecular test to detect Mycobacterium tuberculosis, as well as mutations indicating resistance to rifampicin.
NVP	Nevirapine
RAL	Raltegravir
RPV	Rilpivirine
RTV	Ritonavir
TAF	Tenofovir alafenamide
TDF	Tenofovir desoproxil
AlAT	Alanine aminotransferase
Anti HBcorAg	Antibodies to hepatitis B virus nuclear antigen
Anti HBsAg	Antibodies to hepatitis B virus surface antigen
ARVP	Antiretroviral drug
ART	Antiretroviral therapy
AsAT	Aspartate aminotransferase
BC	Bacterioscopic examination of sputum
TANK	Biochemical analysis of blood
VGD	Hepatitis D virus
HBV	Hepatitis B virus
VGN	The upper limit of the norm
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus

EXT	Viral load
VSVI	Inflammatory syndrome of restoration of immunity
PrEP	Pre-exposure prophylaxis
DNA	Deoxyribonucleic acid
Digestive tract	Gastrointestinal tract
IB	Immune blotting
IHD	Coronary artery disease
AI	Integrase inhibitors
UI	Protease inhibitors
STIS	Sexually transmitted infections
ELISA	Enzyme-linked immunosorbent assay
IHLA	Immunochemiluminescence assay
IHA	Immunochromatographic analysis
CT	Computed tomography
KFK	Creatine phosphokinase
PLHIV	People living with HIV (HIV-positive)
HDL	High-density lipoproteins
LDL	Low-density lipoproteins
POPPY	Mycobacteriumavium complex
MLU	Multidrug resistance
INN	International nonproprietary name
MRI	Magnetic resonance imaging
MSM	Men who have sex with men
NRTI	Nucleoside/nucleotide inhibitors of the reverse Transcriptases
NNRTIs	Non-nucleoside reverse transcriptase inhibitors
OAK	Complete blood count
OAM	Urinalysis
OI	Opportunistic infections
ARRESTER	Acute renal failure
Surfactants	Psychoactive substances
PML	Progressive multifocal leukoencephalopathy
PHC	Primary health care
DAA	Direct-acting antiviral drugs
PCR	Polymerase chain reaction
RCTs	Randomized Clinical Trial
RNA	Ribonucleic acid
RNGA	Indirect hemagglutination reaction
RPGA	Direct hemagglutination reaction
AIDS	Acquired immunodeficiency syndrome
CCZ	Cardiovascular diseases
UD	Level of evidence

ULTRASOUND	Ultrasound examination
EGD	Fibrogastroduodenoscopy
CMV	Cytomegalovirus
CNS	Central nervous system
ELECTROCARDIOGRAM	Electrocardiogram, electrocardiography
ET	Rapid test
EHLA	Electrochemiluminescence analysis

1.4 Protocol users: general practitioners, therapists, infectious disease specialists, laboratory specialists, TB specialists, obstetrician-gynecologists, cardiologists, ophthalmologists, neuropathologists, psychiatrists, narcologists, dermatovenerologists, psychotherapists, pharmacologists, nephrologists, gastroenterologists.

1.5 Category of patients: adults, pregnant women.

1.6 Scale of the level of evidence:

And	A high-quality meta-analysis, a systematic review of RCTs, or a large RCTs with a very low probability (++) of bias, the results of which can be extended to the relevant Population.
In	A high-quality (++) systematic review of cohort or case-control studies or a high-quality (++) cohort or case-control studies with very low risk bias or low-risk RCTs (+) risk systematic errors, the results of which can be extended to the relevant population.
With	A cohort or case-control study or a controlled trial without randomization with a low risk of bias (+) whose results can be generalized to an appropriate population, or RCTs with very low or low risk of bias (++ or +) whose results may not be directly distributed to the relevant population.
D	Description of a series of cases or uncontrolled research or opinion Experts.

1.7. Definition [1]**: HIV infection is** a chronic infectious disease caused by the human immunodeficiency virus, characterized by a specific lesion of the immune system and leading to its slow destruction before the formation of acquired immunodeficiency syndrome.

1.8 Clinical classification [2]:

Clinical stages of HIV infection according to the WHO classification in adults.

Clinical stage 1:

- asymptomatic course of HIV infection;
- persistent generalized lymphadenopathy.

Clinical stage 2:

- unexplained moderate weight loss (<10% of estimated or measured body weight);
- recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis);
- shingles;
- angular cheilitis;
- recurrent oral ulcers ;
- itchy papular (or other) rash;
- onychomycosis;
- seborrheic dermatitis.

Clinical Stage 3:

- unexplained severe weight loss (>10% of estimated or measured body weight);
- unexplained chronic diarrhea lasting more than a month;
- unexplained persistent fever (intermittent or persistent, lasting more than a month);
- persistent candidal stomatitis;
- hairy leukoplakia of the oral cavity ;
- pulmonary tuberculosis;
- severe bacterial infections (e.g., pneumonia, empyema, purulent myositis, bone and joint infections, meningitis, bacteremia);
- acute ulcerative-necrotic stomatitis, gingivitis or periodontitis;
- unexplained anemia (<80 g / l); neutropenia (<0.5 x 10 9/L) and/or chronic thrombocytopenia (<50 x 10^9/L).

Clinical stage 4:

- HIV-related cachexia syndrome ;
- Pneumocystis pneumonia;
- severe recurrent bacterial pneumonia;
- chronic herpes (orolabial, genital or anorectal lasting more than a month or visceral of any localization);
- candidal esophagitis (or candidiasis of the trachea, bronchi or lungs);
- extrapulmonary tuberculosis;
- Kaposi's sarcoma;
- cytomegalovirus infection (retinitis or damage to other organs);
- toxoplasmosis of the central nervous system;

- HIV encephalopathy;
- extrapulmonary cryptococcosis, including meningitis;
- disseminated infections caused by atypical mycobacteria;
- progressive multifocal leukoencephalopathy;
- chronic cryptosporidiosis
- chronic isosporiasis;
- disseminated fungal infections (extrapulmonary histoplasmosis, coccidioidosis);
- brain lymphoma or B-cell non-Hodgkin's lymphoma;
- HIV-associated nephropathy;
- HIV-associated cardiomyopathy with clinical manifestations;
- recurrent sepsis (including salmonellosis);
- invasive cervical cancer ;
- atypical disseminated leishmaniasis.

II. METHODS, APPROACHES AND PROCEDURES FOR DIAGNOSIS AND TREATMENT

[3 - 10] :

2.1 Diagnostic criteria [3 - 5]:

Complaints: there are no characteristic complaints, prolonged fever, weight loss, swollen lymph nodes are possible.

At the initial treatment, the patient is provided with psychosocial counseling about HIV-positive status. The patient signsthe certificate of a confidential interview, form No. 095/y (order of the Ministry of Health of the Republic of Kazakhstan No. 175 dated 10/30/2020). Active screening for tuberculosis is carried out for four clinical symptoms: cough, fever, night sweats and weight loss. Further, screening for tuberculosis is carried out at each patient's visit.

History: The disease begins gradually.

Epidemiological history: The source of HIV infection is an infected person who is at any stage of the disease, including during the incubation period. Analysis of the degree of contact with persons with similar diseases, taking into account the mechanism and route of transmission.

Table 1. Doclevel of HIV transmission

Transmission pathways	**Characteristic**	**UD***
Sexual	sexual contact with an infected partner with detectable viral load	In
Parenteral	non-medical and medically invasive procedures, blood transfusions, transplantation of organs, tissues and cells	In

Vertical	from an HIV-infected mother to her child during pregnancy, childbirth, after childbirth	In

*Note - *level of evidence*

Predisposing factors:

- signs of severe immunodeficiency in an HIV-infected partner.

Table 2. Classification of HIV-associated immunodeficiency

Classification of HIV-associated immunodeficiency	CD4 lymphocyte levels in patients of different ages			
	≤ 11 months (%)	12—35 months (%)	36—59 months (%)	≥ 5 years (in cl/μl)*
Negligible	>35	>30	>25	>500
Temperate	30—35	25—30	20—25	350—499
Expressed	25—29	20—24	15—19	200—349
Heavy	<25	<20	<15	<200 or <15%

* *Including teens and adults*

- high viral load in an HIV-infected partner;
- advanced clinical stage in an HIV-infected partner.

Risk factors :

- the presence of sexually transmitted diseases;
- contact with the biomaterial of an HIV-infected person in the presence of damage to the skin and mucous membranes;
- unprotected sex ;
- the use of non-sterile medical and non-medical instruments for invasive interventions;
- blood transfusion, transplantation of organs, tissues, cells;
- perinatal contact of the child with an HIV-infected mother during gestation, childbirth and breastfeeding.

Physical examinations:

- weight loss - weight loss (<10%), severe weight loss (>10%), cachexia;
- body temperature (fever for more than a month);
- respiratory rate (dyspnea at rest);
- swollen lymph nodes ;
- dermatitis, vesicular, papular rashes;
- retinitis;
- stomatitis, ulcerative-necrotic lesions, proliferation of the oral mucosa, mainly lateral over thetongue;

- cough, shortness of breath, wheezing;
- cardiomyopathy;
- nephropathy;
- diarrhea, enlargement of the liver and spleen, dysphagia;
- Signs of the following diseases: infection caused by the human papillomavirus (genital warts of the genitals and anus, cervical cancer);
- impaired cognitive functions (Appendix 1), paresis, symptoms of neuropathy, impaired consciousness,meninegial syndrome;

Laboratory tests:
General blood test: leukopenia, lymphocytosis, increased ESR or C-reactive protein, anemia, thrombocytopenia.

General urinalysis: proteinuria, cylindruria.

Biochemical blood test:
- increased levels of creatinine and urea in the blood, hyponatremia, hypokalemia (with the development of AKI);
- increased fasting glucose levels;
- increased cholesterol (HDL, LDL);
- increased triglycerides;
- increased lipase;
- increased amylase;
- increased activity of transaminases;
- increased alkaline phosphatase;
- increased lactate dehydrogenase.

Serological blood test :
- enzyme-linked immunosorbent / immunochemiluminescence / immunochromatographic / electrochemiluminescence assay for HIV (ELISA/IHLA/IHA/ECHOLA);
- immunoblotting or chromatographic test with protein profile to confirm the diagnosis of HIV;
- enzyme-linked immunosorbent / immunochemiluminescence / immunochromatographic / electrochemiluminescence assay for hepatitis C (antiHCV) and hepatitis B (HBsAg, anti HBsAg, anti HBcorAg,);
- determination of total antibodies to Treponema pallidum in blood serum by ELISA method.

Polymerase chain reaction:

- quantitative determination of HIV RNA in blood plasma (determination of viral load);
- determinationof HIV drug resistance to antiretroviral drugs by genotyping;
- qualitative determination of HCV RNA by PCR with positive ELISA/IHLA/IHA/ECLA for anti-HCV;
- qualitative determination of HBV DNA by PCR with positive ELISA/IHLA/IHA/ECLA for HBsAg;
- testing for carriage of the HLA-B*5701 allele prior to administration of Abacavir-containing ART regimens.

Immunophenotyping:
- determination of the number of CD4 lymphocytes (absolute and percentage).

Histopathology and cytology:
- cytological examination of a smear from the cervix, a PAP test or a cytological examination of a smear from the cervix on a liquid cytology machine.

HIV testing by rapid diagnostic methods (rapid testing):
- express testing for HIV, followed by examinationin ELISA / IHLA / ECLA of pregnant women who were admitted to childbirth without the results of a double examination for HIV infection, or examined once for more than 3 weeks before admission to perinatal centers (maternity wards). Those admitted to childbirth belonging to key groups, or whose sexual partner is HIV-infected, or a user of injecting drugs drugs examined more than 3 weeks before admission to the perinatal center (maternitydivisions). In case of a positive result of rapid testing in childbirth, biological material for examination by the ELISA / ICHLA / ECLA method is delivered to the laboratory of the health care organization operating in the field of HIVprevention within 12 hours;
- victims in emergency situations in contact with infected body fluids;
- key populations (people who inject drugs, sex workers, men who have sex with men, transgenderpeople) are examined anonymously in health care organizations, regardless of ownership, and in non-governmental organizations as part of triage testing;

- sexual/injectable HIV-seronegative partners of PLHIV (without ART and/or without virologic suppression) are examined 1-2 times a year, including with the use of rapid tests for self-testing;

Medical organizations providing obstetric care to pregnant women and medical organizations in which there is an occupational risk of HIV infection plan and purchase rapid tests (ET) in a timely manner for diagnosing HIV in pregnant women during childbirth and post-exposure prophylaxis for medical workers with daily accessibility;

Public health organizations working in the field of HIV prevention plan and purchase antiretroviral drugs and rapid tests (ETs) in a timely manner for pre- and post-exposureprophylaxis with round-the-clock availability for the population, key groups and sexual/injecting partners of PLHIV.

Additional laboratory research methods in the presence of clinical signs of HIV-associated diseases:

- manual microscopy of scraping from the oral cavity ;
- determination of hepatitis C virus in biological material by the method of P C R quantitative;
- determination of the genotype of the hepatitis C virus by PCR;
- determination of hepatitis B virus in biological material by the method of P C R quantitative;
- detection of Toxoplasma gondii in biological material by PCR qualitatively;
- detection of Toxoplasma gondii in biological material by PCR quantitative;
- detection of herpes simplex virus types 1 and 2 in biological material by PCR qualitatively;
- detection of herpes simplex virus types 1 and 2 in biological material by the method of P C R quantitative;
- detection of cytomegalovirus (HSV-V) in biological material by PCR qualitatively;
- detection of cytomegalovirus (HSV-V) in biological material by quantitative PCR;
- detection of Mycoplasma pneumoniae in biological material by PCR;
- immunochromatogris aphaic / immunochemiluminescence /enzyme-linked immunosorbent / electrochemiluminescence assay for the determination of cryptococcal infection antibodies (ICA/IHLA/ELISA/ECHOLA).

Table 3: Level of evidence of laboratory research methods

Method	Testimony	UD*
Hematology	Patients with clinical criteria for HIV infections to determine the severity .	With
Biochemical	Patients with clinical criteria for HIV infections to determine the severity .	With
Serological (ELISA/IHLA/IHA/ EHLA/IB)	Patients with clinical criteria for HIV infection to determine nosology.	B
Molecular-genetic (PCR)	Patients with clinical criteria for HIV infection to determine nosology and ART monitoring.	B

Note - *level of evidence.

Table 4. The level of evidence of instrumental research methods:

Method	Testimony	UD*
Organ X-rays chest	All patients at the dispensary accounting and then at least once a year.	With
Ultrasound of the abdominal organs	Patients with clinical symptoms of HIV infection to clarify the size of the enlargement of the liver, spleen, lymph nodes and assessment of their structure.	With
Elastography (elastometry) of the liver	Patients with chronic viral hepatitis (B or C) planning to undergo antiviral therapy (to assess fibrosis before, during, and after); patients with cirrhosis of the liver	With
Chest X-ray	Patients with clinical symptoms of HIV infection with auscultatory changes in the lungs, if pneumonia is suspected, tuberculosis.	With
EGD	Patients with clinical symptoms of HIV infection with changes in the mucous membrane in the larynx, esophagus, abdominal organs.	In
MRI/CT	Patients with clinical symptoms of HIV infections according to indications.	In
Colonoscopy	Patients with clinical symptoms of HIV infections with changes in the mucous membrane of the large intestine.	In
ELECTROCARDIOGRAM	Patients with clinical symptoms of HIV infections, with auscultatory changes in	With

	heart to clarify dysfunction conduction and trophism of heart tissue.	
Initial Xpert MTB/RIF test	Patients with clinical symptoms of HIV infections, tuberculosis for the diagnosis of tuberculosis.	In
Cervical cancer screening Uterus.	Female patients 15–49 years of age, consisting of at the dispensary registration 1 time per year.	With

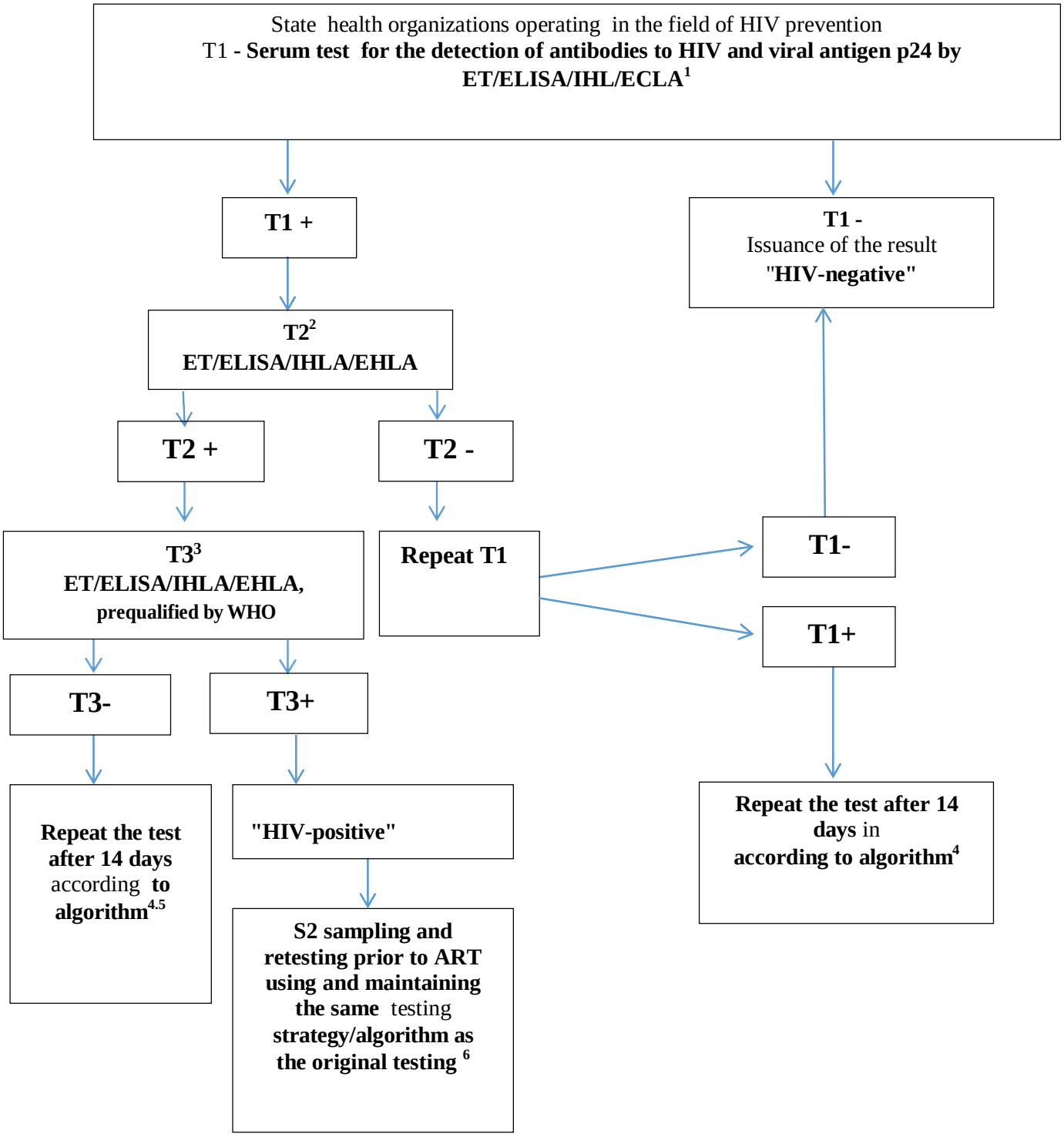
Note - *level of evidence

Indications for specialist consultation :

- consultation with a TB specialist - when registering, with signs / suspicion of tuberculosis, MAC complex;
- consultation with a neurologist - with signs / suspicion of cryptococcal meningitis, HIV encephalopathy, toxoplasmosis of the central nervous system, PML, brain lymphoma, peripheralpolyneuropathy;
- consultation with a psychiatrist / narcologist - in case of signs / suspicion of a mental disorder, HIV encephalopathy / dementia, depression, drug and alcohol dependence (PAS);
- consultation of a psychotherapist (psychologist) - with psychological problems;
- consultation with an ophthalmologist - in case of signs / suspicion of retinitis;
- consultation with a cardiologist - in case of signs / suspicion of cardiomyopathy, cardiovascular diseases;
- consultation with an oncologist - in case of signs / suspicionof a malignant neoplasm;
- consultation with a gynecologist - for women when registering, then at least once a year, with signs / suspicion of gynecological diseases, cervical cancer;
- consultation with a therapist - in the presence of another somatic pathology;
- consultation with a dermatovenereologist - when registering, then in case of signs / suspicion of skin and venereal diseases;
- consultation with an endocrinologist - in case of signs / suspicion of endocrinological diseases;
- Consultation with a nephrologist - if there are signs / n of suspicion of kidney disease.

The recommended surveys and the frequency of follow-up are reflected in Annex 2 to the Protocol.

Algorithm Lab Diagnostics HIV infection y Adults.

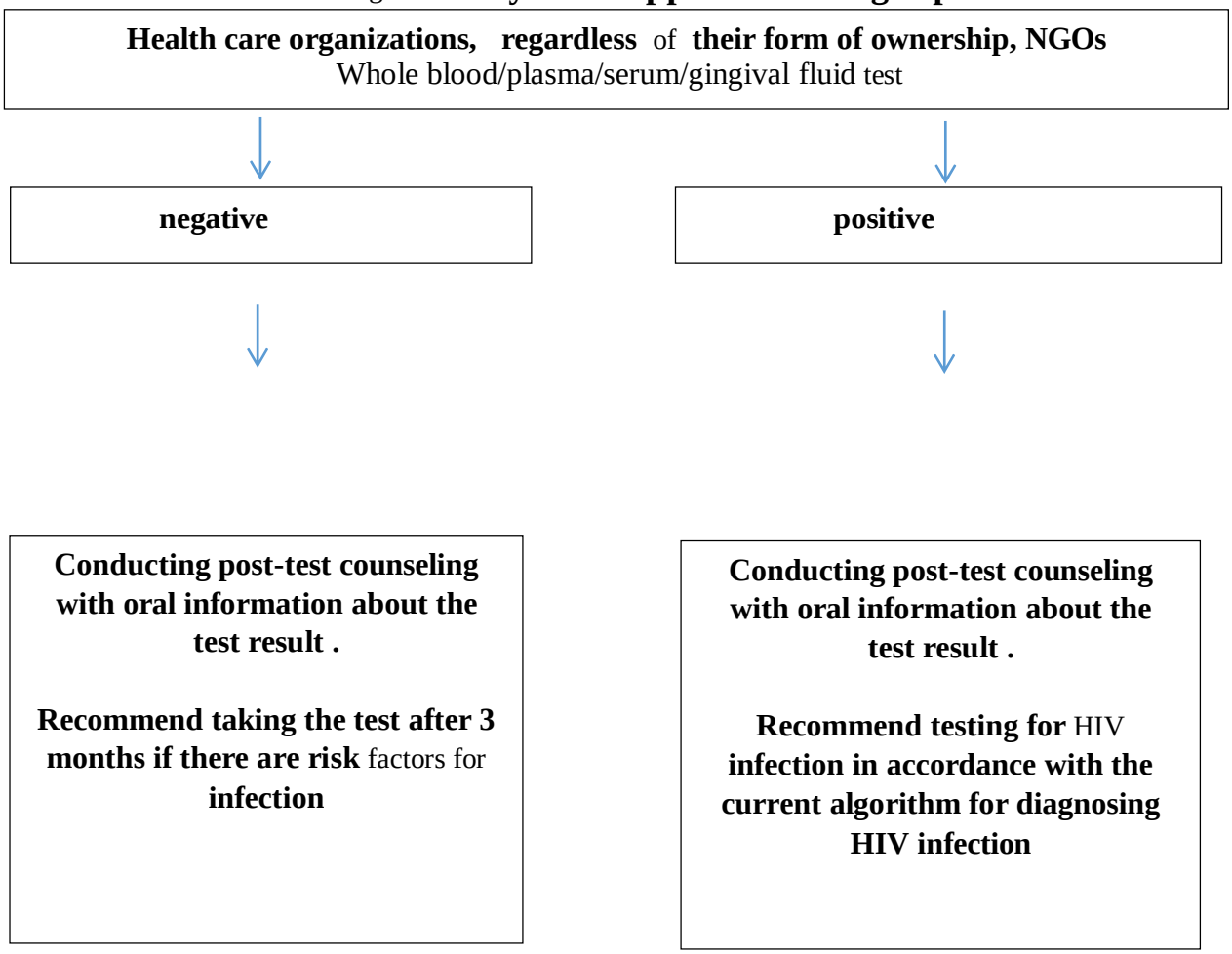


[1] a serum sample for HIV testing is transported to the laboratories of healthcare organizations operating in the field of HIV prevention at a temperature of +2°- +8°C within 2 working days from the date of blood collection; At the initial examinationAntibodies to HIV of the first and second types and the viral antigen p24 are simultaneously determined by enzyme-linked immunosorbent assay (hereinafter referred to as ELISA) or immunochemiluminescence analysis (hereinafter referred to as T1) – IHLA), or electrochemiluminescent Analysis (more – EHLA) c Using test-

Systems c Diagnostic Sensitivity– 100 % (lower limit 95 % Trust Interval
– not less than 99%); diagnostic specificity – not less than 99% (the lower limit of 95% of the confidence interval is not less than 98%); analytical sensitivity of no more than 2 IU / ml (minimum amount of p24 antigen), or using fourth-generation rapid tests with sensitivity and specificity, confirmed by the requalificationof the World Organization Health.
The study of primary-positive/doubtful blood samples received from blood centers is carried out by the IHLA / ECLA method or on automated ELISA analyzers.
2 the second study (T2) is carried out using a test system that differs from T1. The use of third- and fourth-generation HIV tests is allowed. If T1 was performed using a rapid test, then retesting (T2) is carried out using the laboratory method ELISA / ICHLA / ECHOLA;
[3] The third study is carried out using a method that was not used in the first (T1) and second (T2) studies, since the reliability of the diagnosis is ensured by a combination of various methods and reagents used in the examination.
[4] Upon receipt of a second (after 14 days) dubious result for HIV, additional studies are carried out to quantify HIV RNA with a test sensitivity of no more than 50 copies / ml.
[5] Upon receipt of two doubtful test results, a blood sample (S2) is sent to the laboratory of the KSCDIZ for additional research by immune, linear blot or molecular biology.
6 If the HIV status does not change after re-testing, then the HIV-positive status of the examined person is considered confirmed. If the HIV status changes after re-testing, then a commission S3 is taken and the sample is sent for supplemental testingto the laboratory of the KSCDIZ.

Algorithm

HIV testing of anonymous applicants using rapid tests



2.3 Differential diagnosis and justification of additional studies:

Disease	Similar symptoms	Distinctive symptoms	Laboratory tests
Infectious mononucleosis	Lymphadenopathy, tonsillitis, hepatolienal syndrome, fever	Duration no more than 1 month, prevails systemic swollen lymph nodes.	Positive Paul-Bunnel test. In the blood, atypical mononuclear cells are more than 10%.
Rubella	Enlargement of occipital lymph nodes, exanthema	Epidanamnesis, short-term symptoms, affects only the occipital lymph nodes.	Antibodies to rubella virus in increasing titer.
Toxoplasmosis	Encephalitis, lymphadenopathy, hepatomegaly, jaundice, exanthema.	Epidanamnesis, chorioretinitis, calcifications in the brain , visceral lesions.	Serology (ELISA IgM, IgG, avidity of IgG antibodies), PCR, CT/MRI of the brain
Acute meningoencephalitis (viral, bacterial etiology).	Meningeal, encephalic syndrome, poliomyelitis-like syndrome	Epidanamnesis, the clinical picture is more clearly delineated , with bacterial non-meningococcal meningitis - the presence of foci Infectionsand.	Microbiology, serology, virology, immunofluorescence diagnostic method
Adenovirus infection	Fever, nasopharyngitis, lymphadenitis	Epidanamnesis, acute course, lymphadenitis predominantly regional lymph nodes	Virology, serology with increasing AT titer, immunofluorescence study, hemogram.
Enterovirus infection	Fever, exanthema, polyadenia, hepatolienal syndrome, encephalitis.	Herpangina, diarrhea, lymphadenitis is less pronounced.	Serology in increasing titer.
Sepsis	Fever, intoxication, multiple organ manifestations, exanthema, meningitis, otitis, sinusitis, Pneumonia.	The presence of a primary focus (skin, lungs, intestines, etc.)	Isolation of the pathogen from the blood and other material, negative ELISA for HIV, hypogammaglobulinemia, normal amount of CD4.
Chronic viral hepatitis	Decreased appetite, enlargement of the liver, spleen, polyadenia, jaundice.	Connection with viral hepatitis, symptoms are moderately pronounced, Polyorgan is not characteristic.	Markers of VH (A, B, C, D) in blood serum, PCR, decrease in CD8, CD4 level is normal.

Intestinal infection, salmonellosis (generalized form).	Diarrhea, weight loss, fever, intoxication, the presence of foci in other organs (meningitis, pneumonia)	Generalized forms develop only in children of the first months of life Premorbid background is burdened, often nosocomial infection	Cultures of feces, blood, serology (RPGA)
Helminthic infestations.	Loss of appetite, lethargy, weight loss, diarrhea, Polyadenia	Epidemiology, malabsorption syndrome is not Characteristic.	Detection of helminth larvae in feces, duodenal contents, sputum, urine.
Tuberculosis	Polyadenia, intoxication, lung damage, central nervous system, fever, weight loss, weakness, hepatolienal syndrome.	Epidanamnesis, the presence of a primary complex in the lungs	Bacteriology - isolation of MBT from sputum, other biological fluids, organs and tissues, Xpert MTB / RIF, X-ray examination of the lungs (foci, cavities).
Mumps and mumps of other etiology.	Enlargement of the parotid salivary glands	With mumps: occurs acutely, passes within 10 days, other salivary glands, orchitis, pancreatitis may be involved. With a tumor, salivary stone Diseases are a one-sided process.	Serological studies with an increase in antibody titer (RNGA). X-ray research methods.

III. TACTICS OF TREATMENT AT THE OUTPATIENT LEVEL [3 - 10]:

The course of treatment with ART is lifelong, at the outpatient level, a scheme with two or more drugs is used, the frequency ofARV drugs depends on the form of release. Preference is given to combined drugs in fixed dosages with a single daily dose.

Prior to the initiation of ART, an assessment of the readiness of HIV-infected patients to start and continue AR T is carried out, in accordance with Annex 3 to the Protocol.

All people newly diagnosed with HIV should be retested to confirm their HIV status before starting ART, using the same testing strategies and algorithm as the baseline diagnosis.

3.1 Non-drug treatment:

Regimen, diet: depends on the defeat of individual systems and organs.

3.2 Drug treatment:

ART should be started in patients with HIV infection, regardless of the clinical stage of the disease, with any number of CD4 cells, no later than 7 days from the time of diagnosis.

Prior to initiating APT, it is recommended to perform a genotypic resistance test, preferably immediately after the diagnosis of HIV. Genotypic testing should not delay the initiation of ART (it can be adjusted based on the results of genotypic testing).

If it is necessary to start APT before the results of the resistance test are available, it is recommended that adrug with a high genetic barrier to resistance (for example, IP/B or second-generation AI) be included in the first-line treatment regimen

The decision whether to offer a patient a rapid start of APT, possibly on the day ofdiagnosis, or postpone until further tests are performed, depends on theconditions of the medical institution and condition patient, clinical indications for faster initiation of APT and the risk that the patient may drop out of the surveillance system in a medical institution. To reduce the time it takes for a patient to "lose" betweendiagnosis and initiation of APT, it is necessary to remove structural barriers that affect this process.

Etiotropic therapy:

NRIOT:

- abacavir (ABC) 300 mg; 300 mg 2 times a day;
- zidovudine (ZDV or AZT) 100 mg , 300 mg; 300 mg 2 times a day;
- zidovudine (ZDV or AZT) 10 mg/1ml, intravenous 2 mg/kg followed by intravenous infusion of 1 mg/kg/hour prior to delivery;
- lamivudine (3TC) 100 mg, 150 mg ; 150 mg 2 times a day;
- tenofovir (TDF) 300 mg; 300 mg 1 time per day;
- tenofovir alafenamide (TAF) 25 mg; 25 mg 1 time per day.

NNRTI:

- efavirenz (EFV) 200 mg, 600 mg , 400 mg ; 400-600 mg 1 time per day;
- etravirine (ETV) 100 mg , 200 mg; 200 mg 2 times a day;
- rilpivirine (RPV) 25 mg , 25 mg 1 time per day;
- * doravirin (DOR) 100 mg, 1 time per day.

UI:

- lopinavir/ritonavir (LPV/r) 200/50 mg; 200/50 mg 2 times a day;
- darunavir (DRV) 400 mg, 600 mg, 800 mg; 600 mg 2 times a day in combination with ritonavir or cobicistat at a dose of 100 mg 2 times a day , at a dose of 800 mg 1 time per day.
- * atazanavir (ATV) 300 mg with ritonavir or cobicistat at a dose of 100, 150 mg once a day.

AI:

- raltegravir (RAL) 100 mg , 400 mg; 400 mg 2 times a day;
- dolutegravir (DTG) 50 mg; 50 mg 1 time per day;
- * bictegravir (BIC) 50 mg , 50 mg 1 time per day;
- * elvitegravir (EVG) 150 mg in combination with cobicistat 150 mg, 1 time per day.
- * long-acting cabotegravir (CAB-DD) 200 mg / ml - the first 2 injections are administered at intervals of 4 weeks, and then every 8 weeks. **Combination drugs in fixed dosages:**
- abacavir/lamivudine (ABC/3TC) 600/300 mg; 1 time per day;
- zidovudine/lamivudine/abacavir (AZT/3TC/ABC) 300/150/300 mg; 2 times a day;
- tenofovir/emtricitabine (TDF/FTC) 300/200 mg; 1 time per day;
- tenofovir/emtricitabine/efavirenz (TDF/FTC/EFV); 300/200/600 mg, 1 time per day;
- zidovudine/lamivudine (AZT/3TC); 300/150 mg, 2 times a day;
- abacavir/lamivudine/dolutegravir (ABC/3TC/DTG) 600/300/50 mg; 1 time per day;
- darunavir / cobicistat / tenofovir alafenamide / emtricitabine (DRV / S / TAF / FTC), 800/150/200/10 mg, 1 time per day;
- tenofovir/emtricitabine/rilpivirine (TDF/FTC/RPV); 300/200/25 mg, 1 time per day;
- tenofovir alafenamide/emtricitabine/rilpivirine (TAF/FTC/RPV); 25/200/25 mg, 1 time per day;
- tenofovir/lamivudine/dolutegravir (TDF/3TC/DTG); 300/150/50 mg, 1 time per day;
- * tenofovir alafenamide / emtricitabine / bictegravir (TAF / FTC / BIC) 25/200/50 mg, 1 p perday;
- * tenofovir alafenamide / emtricitabine / elvitegravir / cobicistat (TAF / FTC / EVG / c) 10/200 / 150 / 150 mg, 1 time per day;
- * tenofovir / emtricitabine / elvitegravir / cobicistat (TDF / FTC / EVG / c) 300/200/150/150 mg, 1 time per day;
- * dolutegravir / rilpivirine, 50/25 mg, 1 time per day;
- * dolutegravir / lamivudine, 300/50 mg, 1 time per day.
- * cabotegravir / rilpivirine, 200 mg / ml / 300 mg / ml, IM 1 time in 2 months.

**after registration in the territory of the Republic of Kazakhstan.*

Table 5. The main regimens of first-line antiretroviral therapy .

	Combination of NRTI	

	The first drug	The second drug	Third preparation
Preferred scheme	3TS (or FTC)	TDF (or TAF)	DTG[a]
	3TS (or FTC)	TDF (or TAF)	BIC[b]
	3TS	ABC[e]	DTG[a]
Alternative schemes	3TS (or FTC)	TDF	EFV[c] (400, 600 mg)
	3TS (or FTC)	ABC[e] (or TDF)	RAL
	3TS (or FTC)	TDF (or TAF)	DOR
	3TS (or FTC)	TDF (or TAF or ABC[e])	DRV/sec or DRV/r
	3TS (or FTC)	TDF (or TAF)	RPV
	3TS	DTG[a]	
	.CAB	RPV	

[a]DTG can be used by women and adolescent girls of childbearing potential as long as they are aware of the benefits and risks of taking this drug.

[b]BIC should not be used in conjunction with rifampicin and St. John's wort.

[c]EFV is not prescribed to persons with a history of severe mental illness .

[e]ABC is contraindicated if HLA-B*57:01 is positive. Even if HLA-B*57:01 is negative, consultation on MIRV is mandatory. ABC should be used with caution in patients with a high risk of CVD (> 10%), with a negative result on HBsAg.

It is possible to use RPV instead of EFV. The combination of TDF / FTC / RPV (TDF + FTC + RPV) IS USED IN PATIENTS WITH AN HIV RNA LEVEL OF ≤ 100,000 COPIES / ML, CD4 count> 200 cells / μl, not on drugs that increase the pH of the stomach.

The 3TC+DTG regimen is used for HIV VN <500,000 copies/ml, not recommended after ineffective PrEP

Treatment regimens with EFV are taken at bedtime or 2 hours before dinner.

DRV/s or DRV/r are taken with food.

AI or TAF therapy may be associated with weight gain.

There are generic forms of TDF that contain phosphate, maleate and succinate salts instead of fumarate salts. They are interchangeable. Where possible, combination preparations containing TDF may be replaced by combinationpreparations containing TAF. When combined with drugs that inhibit P-glycoprotein, TAF is prescribed at a dosage of 10 mg; with drugs that do not

inhibit P-glycoprotein, TAF is prescribed at a dosage of 25 mg. The decision to use TDF or TAF depends on the individual characteristics and availability of the drug. If the APT regimen does not include a booster, TAF and TDF have a similar short-term risk of adverse events to the kidneys leading to discontinuation of treatment and bone fractures. TAF should be preferred over TDF in patients with:
- established or high risk of CKD,
- combinedwith drugs toxic to the kidneys, or previous toxicity of TDF,
- osteoporosis / progressive osteopenia, high FRAX scores or risk factors,
- history of fractures .

RAL can be taken as 400 mg 2 p / day or 1200 mg (two tablets of 600 mg) 1 p / day. RAL 1 p / day should not be used in the presence of an inducer (for example, anti-tuberculosis drugs, antiepileptic drugs) or divalent cations (for example, to alcium, magnesium, iron); in such cases, RAL 2 r / day should be used.

HIV infections that occur when PrEP fails may be associated with mutations associated with resistance. 3TC/DTG can only be used in this context in the absence of documented resistance in the genotypic test.

DOR is inactive against HIV-2. DOR has not demonstrated a lack of inferiority compared to AI. In the case of virological failure, there is a risk of mutations associated with resistance.Before starting DOR treatment, the results of a genotypic resistance test are required.

EFV: do not prescribe if there is a history of suicide attempts or mental illness; is not effective against HIV-2 and HIV-1 strains of the O. RPV is not effective in HIV-2. In one large study, there was an increase in the risk of CVD with cumulative use of DRV/r, which was not confirmed in smaller studies. When using boosted regimens with RTV or COBI, there is an increased risk of drug interactions,

There are limited data on the use of TAF with eGFR <10 mL/min.

CAB+RPV are used in patients with HIV VN suppression <50 copies/mL in the last 6 months in the absence of a history of resistance, HBV immunity, or concomitant HBV vaccination in the absence of immunity.

Precautions and nutritional requirements for patients starting ART for the first time are reflected in Annex 4 to the Protocol.

Selected groups of patients:

- pregnant women;
- patients with low (≤ 50 cells/μL) CD4 lymphocyte count;
- patients with neurocognitive disorders, CNS damage;
- patients suffering from chronic kidney disease;
- patients suffering from cardiovascular diseases or at high risk of developing them;

- patients suffering from chronic hepatitis and / or having an elevated level of aminotransferases;
- patients receiving anti-TB drugs;
- patients receiving methadone;
- in emergency situations.

1. Pregnant women:

Preferred ART regimens :

- TDF+3TC (or FTC) + DTG
- ABC+3TC+DTG
- TDF+3TC (or FTC) + RAL 400 mg
- TDF+3TC (or FTC) + DRV/r

Alternative ART schemes :

- ABC+3TC+ RAL 400 mg
- ABC+3TC+ EFV
- TDF+3TC (or FTC) + EFV
- TDF+3TC (or FTC) + RPV

If a woman is registered for pregnancy at the end of the second or third trimester, ART should be started immediately, and, in the case of high VN, consider adding to the treatment regimen AI (DTG, RAL) as the drug of choice to rapidly reduce VN and achieve undetectable VN by the time of delivery.

Women who can be diagnosed with HIV in the third trimester of pregnancy should have a resistance test and consider changing the regimen or adding AI to rapidly reduce VN.

Pregnant women with nausea are often prescribed H2 blockers or proton pump inhibitors. Careful analysis of concomitant medications at each visit and provision of information to pregnant women about potential drug interactions is recommended.

Reducing the impact of RPV in the second and third trimesters; consider more frequent monitoring of HV. RPV is not active against HIV-2.

Pregnant women should be monitored once a month or once every two months (depending on the adherence and duration of virologic suppression) and as close as possible to the expected date of delivery. HIV VN should be tested every two months of pregnancy and include 36 weeks of gestation.

Options for the use of **ARV drug regimens in pregnant women who first sought help at the time of delivery** (who did not receive ARV therapy during pregnancy):

• In / in ZDV *: during labor and delivery: a loading dose of 2 mg / kg followed by an intravenous infusion of 1 mg / kg / hour before delivery.
Consider administering a loading dose, then proceed to delivery, if possible, do a cesarean section.

- If the result of a rapid HIV test is positive during childbirth, in the absence of intravenous ZDV, the woman is prescribed an antiretroviral therapy regimen TDF + 3TC (or FTC) + DTG with informed consent.

Method of delivery

Women with HIV VN ≤50 copies/ml – natural delivery.

Women with HIV VN> 50 copies/mL at 34-36 weeks:

- planned cesarean section at 38 weeks;
- intravenous ZDV: during labor and delivery : a loading dose of 2 mg / kg followed by an intravenous infusion of 1 mg / kg / hour before delivery;
- planned cesarean section: start intravenous ZDV 3 hours before surgery;
- Unscheduled caesarean section: Consider administering a loading dose, then proceed to delivery.

Women diagnosed with HIV during childbirth:

- if possible, perform a cesarean section;
- In / in ZDV: during labor and delivery: a loading dose of 2 mg / kg followed by an intravenousinfusion of 1 mg / kg / hour before delivery;
  Consider administering a loading dose, then proceed to delivery.

Feeding a newborn

The topic of feeding should be discussed with the pregnant woman as early as possible during pregnancy, along with providing information and support to themother:

- It is recommended not to breastfeed, as this is the best way to prevent transmission from mother to child;
- feed infants born to mothers living with HIV with formula;
- To reduce the potential physical and emotionaldiscomfort associated with breast engorgement as well as the risk of covert breastfeeding, women living with HIV should be given cabergoline to suppress lactation after childbirth;
- If a woman chooses to breastfeed, a monthly observation is recommendedthroughout the breastfeeding period, with enhanced clinical and virological monitoring of both mother and child;
- in case of HIV VN in the mother>50 copies / ml it is recommended to stop breastfeeding, providing the mother with Cabergoline to suppress lactation;
- immediate consultation of specialists is necessary in the presence of signs and symptoms of mastitis, infections of the oral cavity or intestines in an infant;

- After stopping breastfeeding, the baby should undergo the usual diagnosis, which is recommended for children at risk of HIV infection.

2. Patients with initially low (≤ 50 cells/μl) CD4 lymphomacount:
Recommended ART regimens, including:

- DTG or
- DRV/r, or
- DRV/s, or
- LPV/r in combination with ABC or
- TDF + 3TC or
- FTC.

For the treatment of patients with a low level of CD4 lymphocytes, it is recommended to use regimens that include boosted PIs.
As a nucleoside base, it is recommended to use a combination of ABC + 3TC or TDF + 3TC in standard doses (or a combination preparation of TDF / FTC).

3. Patients with neurocognitive disorders, CNS involvement:
The recommended ART regimen includes:
DTG or LPV/r,
or DRV/r, or
DRV/s in combination with AZT/3TC.

Table 6. Ability to penetrate the central nervous system of various antiretroviral drugs in accordance with the CPE scale*

Classes of drugs	4	3	2	1
NRTI	AZT(ZDV)	ABC FTC	3TC	TDF
NNRTIs		EFV	ETV	
UI		DRV/r or DRV/s LPV/r		
AI		RAL DTG		

***the** numbers indicate an assessment of the best penetration into the central nervous system (4 is the best degree of penetration).

4. Patients suffering from chronic kidney disease: Recommended ART regimen:
ABC + 3TC + DTG.

Alternatively, a third drug can be prescribed DRV / c due to the minimaleffect on kidney function.
TDF is not recommended for patients with renal insufficiency.
Patients suffering from kidney disease who are on schemes with TDF are recommended to carry out a monthly calculation of the glomerular filtration rate andcre-athin clearance according to the Cockcroft-Gault formula.
For men (norm 90-150 ml / min) CCF = 1.23 x 140 - age (years) x body weight (kg) blood creatinine (μmol / l)
For women (norm 90-130 ml / min) CCF = 1.05 x 140 - age (years) x body weight (kg) blood creatinine (μmol / l)

5. Patients suffering from cardiovascular diseases or at high risk of developing them:

Recommended ART regimen :

TDF+3TC (or FTC) + RPV (or DTG, or ETV).
It is necessary to annually calculate the risk of developing cardiovascular diseases according to the Framingham scale in men over 40 years of age and women over 50 years of age. A formula specifically designed to assess the risks of CVD in HIV-infected patients: see http://www.chip.dk/Tools

6. Patients suffering from chronic hepatitis and / or having an elevated level of aminotransferases:

Patients with co-infection with HIV infection and chronic hepatitis B, B + D are recommended:

- at a normal level of ALT / AST activity or when it rises no more than 2.5 times higher than the upper limit of normal (ULN) - DTG or EFV or RPV (if there are contraindications to taking EFV and with an HIV RNA level <100,000 copies / ml) in combination with TDF + 3TC or TDF / FTC;
- when the level of ALT or AST activity is more than 2.5 times higher than the ULN – DTG, boosted PIs (DRV/r or DRV/s or LPV/r) in combination with TDF+3TCor TDF/FTC.

HIV infection and CHC:

The optimal combination of NRTIs is TDF+3TC or FTC in standard dosages. If it is impossible to use TDF, ABC is prescribed.
Standard ART regimen for HIV+CHC patients treated with CHC with direct-acting antivirals (DAAs) sofosbuvir and daclatasvir:

- with a normal level of ALT / AST activity or an increase of no more than 2.5 times higher than the highest limit of the norms-RPV (if EFV is present in the ART regimen

dose adjustment of daclatasvir up to 90 mg / day) or DTG (at HIV RNA level >100,000 copies / ml) in combination with ABC or TDF + 3TC or TDF / FTC is required;

- when the level of ALT / AST activity is more than 2.5 times higher than ULN - DTG or boosted PI (DRV / s) in combination with ABC or TDF + 3TC or TDF / FTC.

If bavirin is present in the treatment regimen, it is undesirable to combine with AZT (ZDV).

In patients with a combination of HIV infection and CHC who do not receive treatment with CHC, a combination of AZT (ZDV) + 3TC may be included in the ART regimen. The duration of treatment with DAA depends on the HCV genotype and the degree of fibrosis.

HCV treatment regimens in patients with HCV/HIV co-infection

Preferred HCV treatment regimens with DAAs (except patients previously treated with protease inhibitors or NS5A)				
GT HCV	Treatment regimen	Duration of treatment and use of RBV		
		Without cirrhosis	Compensated cirrhosis	Decompensated cirrhosis, STR class B / C
1 and 4	EBR/GZR	12 weeks(i)		Not recommended
	GLE/PIB	8 weeks	8–12 weeks(ii)	Not recommended
	SOF/VEL	12 weeks		12 weeks with RBV (ix)
	SOF/LDV +/- RBV	8–12 weeks without RBV (iii)	12 weeks with RBV (iv)	12 weeks with RBV (ix)
2	GLE/PIB	8 weeks	8–12 weeks(ii)	Not recommended
	SOF/VEL	12 weeks		12 weeks with RBV (ix)
3	GLE/PIB	8 weeks(v)	8–12 weeks (II,V	Not recommended
	SOF/VEL +/- RBV	12 weeks(vi)	12 weeks with RBV (vii)	12 weeks with RBV (ix)
	SOF/VEL/VOX		12 weeks	Not recommended
5 and 6	GLE/PIB	8 weeks	8–12 weeks(ii)	Not recommended
	SOF/LDV +/- RBV	12 weeks +/- RBV (viii)	12 weeks with RBV (iv)	12 weeks with RBV (ix)
	SOF/VEL	12 weeks		12 weeks with RBV (ix)

EBR = elbasvir GLE = glecaprevir GZR = grazoprevir LDV = ledipasvir PIB = pibrentasvir

RBV = ribavirin SOF =
sofosbuvir VEL =
velpatasvir VOX =
voxilaprevir
RAS = Resistance-Associated Mutations

i PLHIV with HT 1a with parent HCV RNA <3 and parent HCV RNA <6 million IU/mL

iv RBV can be omitted in previously untreated or previously treated PLHIV with compensated cirrhosis without baseline NS5A RAS. In patients with RBV intolerance, treatment may be extended to 24 weeks

v The duration of HCV HT 3 treatment in patients with failure of previous treatment with IFN and RBV +/- SOF or SOF and RBV should be 16 weeks.

vi Addition of RBV only in previously treated PLHIV with baseline NS5A RAS, if RAS tests are available; if patients with RBV intolerance, treatment should be extended to 24 weeks without RBV

vii If RAS testing is available and demonstrates the absence of NS5A RAS Y93H, RBV can be omitted in the treatment of previously untreated PLHIV with compensated cirrhosis

viii In PLHIV previously treated (IFN/RBV/SOF regimen), regimen with RBV for 12 weeks or extension of treatment to 24 weeks without RBV

ix In patients with RBV intolerance, treatment may be extended to 24 weeks

7. Patients receiving anti-TB drugs:

All PLHIV diagnosed with TB need treatment for TB and HIV infection, regardless of CD4 cell count.

Anti-tuberculosis treatment is started first, and then ART is prescribed as soon as possible (in the first 8 weeks of treatment).

HIV/TB patients with severe immunodeficiency (CD4 cell count less than 50 cells/μL) should start ART immediately within the first 2 weeksafter starting TB treatment.

In the presence of tuberculous meningitis, initiation of ART should be postponed until the end of the intensive care phase of TB.

At the beginning of ART in patients receiving anti-TB treatment, the preferred NNRTI is EFV, which is given at thesite with two NRTIs.

First-line ART regimens in TB patients include 3TC or FTC and TDF in combination with EFV.

Table 7. Recommended first-line ART regimens in TB patients

Treatment regimen	Comments
Recommended ART regimens for PLHIV with tuberculosis receiving Rifampicin	
3TC (FTC) + TDF + EFV 3TC+ABC+EFV	Two NRTIs + EFVs are the preferred regimen of standard first-line ART in people receiving anti-TB Treatment with rifampicin

3TC (FTC) + TDF + DTG	With rifampicin, it is recommended to prescribe DTG at a dose of 50 mg 2 times a day.
3TC (FTC) + TDF + RAL 3TC+ABC+RAL	With rifampicin, it is recommended to prescribe RAL at a dose of 400 mg or 800 mg 2 times a day.
Recommended ART regimens for PLHIV with tuberculosis receiving rifabutin	
3TC (FTC) + TDF + DRV/r or ATV/r, or LPV/r ABC/ZTS + DRV/r, ATV/r, or LPV/r	

When treating MDR-TB bedaquiline, efavirenz, etravirine and integrase inhibitors in ART regimens should be avoided. Delamanid is more preferred when used with ART. Drug interactions in the treatment of HIV and DR-TB according to the Clinical Protocol for the Diagnosis and Treatment of HIV/TB Co-Infection No. 60 dated March 29, 2019. Keep in mind that the response to APT started with a low CD4 count may be VSI. Prophylactic use of prednisolone for 4 weeks at the time of initiation of APT (prednisolone 30 mg 1 p / day 14 days, followed by 20 mg 1 p/day for 14 days) may prevent paradoxical VES associated with tuberculosis in patients with CD4 <100 cells/μL receiving anti-TB treatment.

8. Patients receiving opioid substitution therapy:

if methadone is used together with NNRTIs or PIs, then its concentration in the blood plasma decreases, which requires correction of methadone:

- EFV – it may be necessary to increase the dose of methadone up to 50%
- LPV/r – it may be necessary to increase the dose of methadone to 50%
- DRV / r - it may be necessary to increase the dose of methadone to 15-25%
- ATV - it may be necessary to increase the dose of methadone to 10%

The concentration of buprenorphine (B) and the active metabolite of norbuprenorphine (N) in the blood plasma decreases if it is used together with NNRTIs and increases when it is combined with some PIs or IS.

- EFV may require dose increase B to 50%, N to 70%
- ETV may require an increase in the dose of B to 25%
- ATV may require a dose reduction of B to 50%, N to 100%
- DRV may require a reduction in the dose of N by up to 50%
- EVG may require a dose reduction of B and N from 35 to 42%
- DTG, RAL, RPV, LPV/r do not affect the metabolism of B and N.

9. Post-exposure prophylaxis:

It is recommended in the following cases:

Subcutaneous or intramuscular penetration with a needle for intravenous or intramuscular injection, or using an intravascular device. At the same time, the status of the source patient is HIV-infected, or a person whose current serostatus is unknown, but there are risk factors for HIV infection.

Damage to the skin with a sharp instrument (lancet, etc.), a needle for intramuscular orsubcutaneous injections, or a surgical needle. Contact> 15 min involving mucous membranes or broken skin. The status of the source patient is HIV-infected.

or vaginal sex. The status of the patient, the source - HIV-infected with a positive result for viremia or serostatus is unknown, but there are risk factors for HIV infection. If an HIV-infected source patient is taking ART, PEP should beinitiated, the HIV VN test should be repeated, and if it is undetectable, PEP may be discontinued.

Receptive oral sex with ejaculation. Source partner status, HIV-positive for viremia.

Sharingconsumables when injecting drugs. The status of the partner's source is HIV-infected. In medical organizations, a responsible person is appointed to coordinate measures aimed at preventing HIV infection, including HIV. prescribing antiretroviral drugs for post-exposure prophylaxis to medical workers together with specialists from a healthcare organization operating in the field of HIV prevention.

Healthcare organizations operating in the field of HIV prevention provide advisory assistance to medical organizations, the population, and key groups on PEP issues.

In the event of an emergency, medical workers immediately reportthis case to the head with registration in the journal (form No. 049 / y) and the transfer of the report in the prescribed form to the health care organization operating in the field of HIV prevention.

Taking ARVs in case of emergency should be started within the first 2 hours, but no later than 72 hours after contact with biological material. The decision to initiate PEP is made taking into account the risk of infection and the HIV status of the participants in the emergency. For the prompt establishment of VI The status of the victim in an emergency situation and the person from whom the infection could occur, as well as the timely start of PCP, the Ministry of Defense should have a stock of rapid tests with round-the-clock availability. PEP is provided in healthcare organizations in the field of HIV prevention.

The duration of taking antiretroviral drugs is 28 days. Persons at risk of HIV infection for the observation period (3 months) are advised to avoid unprotected sex, not to donate blood, its components and preparations of organs and tissues; to stop breastfeeding the child.

Preferred ART regimens :

TDF (or TAF) + 3TC (or FTC) + DTG or BIC

Alternative ART schemes :

TDF (or TAF) + 3TC (or FTC) + RAL or DRV /s (DRV/r)

In the case of sexual contact, it is necessary to carry out a complete screening of sexually transmitted diseases. Conduct a consultation on emergency contraception.

Observation:

- serological examination for HIV, HCV, HBV, pregnancy test (women) within 48 hours after contact, then after 1 and 3 months.
- assessment of the tolerability of the PEP regimen.
- transaminase test, HCV PCR, HCV serological test after one month if the source was HCV positive.

10. Pre-exposure prophylaxis:

PrEP for populations at high risk of HIV infection. HIV testing is done before the start of PrEP and is carried out regularly during PrEP. It is recommended to test for STIs (including VH) at the beginning of PrEP and regularly during the use of PrEP, with the informed consent of the client. PrEP is prescribed with a negative HIV test result and negative screening for symptoms of acute HIV infection, without waiting for the results of the test for STIs, VG, creatinine.

PrEP is recommended for men without HIV whohave sex with men (MSM), as well as for transgender people who do not use a condom every time they have sexual intercourse with casual partners or with HIV-positive partners who do not take therapy . Recent STIs, use of post-exposure prophylaxis, or chemsex may be markers of an increased risk of HIV infection.

It can be offered to HIV-negative heterosexual men and women who are inconsistent in condom use and have multiple sexual partners, among whom there is a high probability of people with HIV infection who are not taking therapy. Pregnant women, sexual partners of PLHIV who do not take therapy or are on therapy without virologicalsuppression. A request from a client for PrEP.

The frequency of HIV testing is every 3 months against the background of PrEP. PrEP can be discontinued if the patient is no longer at high risk of infection, in case of early clinical signs of seroconversion, or a positiveHIV diagnostic test.

Clinicians should suspect acute HIV infection in individuals who have reported risky contact behaviour within 4 weeks prior to the PrEP evaluation (e.g., condom breaked during sex with an HIV-infected partner, relapse of injecting drug use with the use of common injection equipment). When testing for HIV infection in these individuals, clinicians should request a history of nonspecific signs or symptoms of viral infection during the previous month or on the day of assessment: fever, fatigue, muscle pain, rashes, headache pain, pharyngitis, swollen cervical lymphnodes, arthralgia, night sweats, diarrhea. If acute HIV infection is suspected, it is recommended to postpone the onset of PrEP. Preferred PrEP regimens:

INN	**Dose**	**Frequency**	**Side effects**
TDF	300 mg	1 time per day	Headache, back pain , abdominal pain, weakness
FTC/TDF	200 mg/300 mg		
FTC/TAF	200 mg/25 mg		Nausea, vomiting, diarrhea

No antiretroviral regimens should be used for PrEP other than a daily oral dose of TDF, FTC/TDF, or FTC/TAF or bi-monthly CAB injections.

Do not provide oral PrEP as an accelerated partner therapy to people who are not under your supervision.

The 2-1-1 regimen (also called "on demand") is not a daily regimen of PrEP, the doses of oral medications increase depending on the events of sexual contact.

Schemes 2-1-1 when prescribing for MSM:

• 2 tablets 2 to 24 hours before sexual contact (preferably closer to 24 hours)
• 1 tablet 24 hours after the first two-tablet dose
• 1 tablet 48 hours after the first two-tablet dose

Depending on the timing of subsequent sexual intercourse, MSM should be instructed to take the following additional doses:

• If sexual contact occurs the day after taking 2-1-1, take 1 tablet daily for 48 hoursafter the last sexual contact.
• If there is a break of less than 7 days between the last pill and the next sexual contact, resume taking 1 tablet per day.

• If there is a break of ≥7 days between the last pill and the next sexual contact, start again with two tablets.

The 2-1-1 dosage is suitable for MSM who have sex infrequently (no more than once a week) and therefore do not require daily oral PrEP.

If the doctor has chosen a 2-1-1 regimen, then no more than 30 tablets should be prescribed so as not to leave the patient without follow-up and HIV testing. For patients who have sex less than once a week, 30 tablets will be enough for 7 intermittent sexual intercourse.

The 2-1-1 mode should not be prescribed:

- for populations other than adult MSM, as it has only been studied in adult MSM;
- for MSM who are expected to have difficulty adhering to a complex dosing regimen (e.g., adolescents, patients with substance use disorder);
- with FTC/TAF, as its safety and efficacy have not been studied;
- for MSM with active hepatitis B infection due to the risk of liver exacerbations on occasional contact with FTC/TDF.

CAB injections may be particularly suitable for patients with serious kidney disease, for those experiencing symptomswith adherence to oral PrEP, and for those who prefer injections every two months. CAB should not be given to individuals with a history of CAB hypersensitivity reaction.

How to use:

- 600 mg of CAB is injected into the gluteus muscle in men and womenat risk of HIV infection. Do not prescribe other antiretroviral drugs in combination with CAB for PrEP.
- Do not inject CAB into sites other than the gluteal muscles, as the pharmacokinetics of drug absorption when injected into other sites is unknown.
- Do not hand over CAB to patients for home use (until self-administration is approved by WHO).

After the onset of PrEP, patients should be monitored by a doctor every 3 months. 1 month after starting PrEP, your doctor may schedule a consultation to assess and confirm a negative HIV test, assess early side effects, discuss medication difficulties, adherence, and respond for questions, also be in touch by phone. All patients receiving PrEPshould be monitored.

At least once every 3 months, for:

- retesting for HIV and assessing signs or symptoms of acute infection and confirming that patients are still not HIV-positive;
- repeated pregnancy testing for women of reproductive age;
- dispensing drugs for a period of not more than 90 days (until the next HIV test);
- assess and support adherence to treatment and risk reduction behaviors;
- STI testing for sexually active people with signs or symptoms of infection, asymptomatic MSM with a high risk ofSTI recidivities, or multiple sexual partners;
- answering questions and providing any new information about the use of PrEP.

At least once every 6 months, for:

- eCrCl control for individuals aged ≥50 years or who have an eCrCl <90 mL/min at the onset of PrEP.
- prescribing more frequent monitoring or the inclusion of additional tests (e.g., urinalysis for proteinuria) if there are other threats to normal kidney function. An increase in serum creatinine is not a reason to refuse treatment if the eCrCl remains ≥60 mL/min for FTC/TDF or ≥30 for FTC/TAF. If eCrCl is steadily decreasing (but still ≥60 mL/min for FTC/TDF or ≥30 mL/min for FTC/TAF), ask if the patient is taking high doses of NSAIDs or protein powders. Consultation with a nephrologist or other assessment of possible threats to the health of the kidneys may be indicated.
- STI screening behaviors for sexually active adolescents and adults (e.g., syphilis, gonorrhea, and chlamydia for both men and women, even if they are asymptomatic).
- control of triglycerides, cholesterol and weight levels of patients who are prescribed FTC / TAF.

At least once every 12 months, for:

- control of eCrCl in all patients continuing to take PrEP drugs over 30 years of age.

Densitometry or other assessments of bone mineral density (bone health) are not recommended before or during PrEP. However, anyone who has been prescribed PrEP, has a history of pathological fractures due to bone fragility, or who has significant risk factors for osteoporosis, should be referred for consultation and treatment.

When prescribing CAB, patients are seen by a doctor after the first injection after 1 month, and then every 2 months.

When visiting after 1 month afterthe first injection (1 month, second injection), you must:

- repeat the HIV test and check for signs/symptoms of acute infection;
- make a CAB injection;
- answer questions.

At each visit every two months (starting with the third injection - 3 months), you must:

- repeat the HIV test and check for signs or symptoms of acute infection;
- repeat pregnancy testing for women of reproductive age;
- make a CAB injection;
- provide clean needles/syringes and provide access to drug dependence treatment services for PWID;
- provide new information about the CAB.

At least once every 4 months (at every second visit for injection, startingwith the third injection - 3 months) it is necessary:

- Conduct STI screening for MSM and transgender women who have sex with men.

At least once every 6 months (starting from the fifth injection - 7 months) it is necessary:

- To screen for STIs for all heterosexually active women and men.

At least once every 12 months (after the first injection), you must:

- assess the desire to continue PrEP injections .

PrEP can be discontinued for several reasons, including patient choice, changes in life situations leading to a reduced risk of HIV infection, intolerant toxicity, chronic non-compliance with prescribed dosing or scheduled follow-up visits, or HIV infection. How to safely stop and resume daily use of PrEP should be discussed with patients both before the beginning of the PrEP, and after the stop of the PrEP. Protection against HIV infection will decrease 7 to 10 days after stopping daily PrEP use. As some patients become infected with HIV soon after stopping PrEP, alternative methods to reduce the risk of HIV infection should be discussed, including indications for PEP and ways to access it quickly if needed.

After you stop taking PrEP for any reason, your medical record should include the following:

- HIV status at the time of discontinuation of treatment;
- reason for termination;
- non-compliance with medication andreports of risky sexual behavior.

Patients with HBV infection who stop taking PrEP should be closely monitored for hepatitis exacerbations .

Any client who wishes torenew their PrEP after stopping needs to be rescreened, including an HIV test.

Patients who wish to discontinue CAB injections, or those who have missed a month or more of CAB injections, should be advised on:

- how to safely stop or resume CAB injections;
- explain the risk of developing HIV drug resistance during the period of declining CAB levels;
- the need for daily oral PrEP or other effective methods of HIV prevention if a persistent risk of HIV infection is expected;
- if the patient wants to switch to daily oral FTC/TDF or FTC/ TAF, it is necessary to start from 8 weeks after the last injection;
- talk about PCP;
- continue follow-up visits quarterly for 12 months;
- perform HIV tests at each follow-up visit quarterly after discontinuation of CAB injections.

If, on a return visit, the HIV test is questionable:

During the follow-up visit, the patienthas several options for confirming the true HIV status:

- carefully evaluate with the patient their adherence to treatment since the last negative HIV test;
- after a few days, take a new blood sample for repeated laboratory testing for HIV, including hypertension / Ab and quantitative testing.

While the HIV status is confirmed, the doctor has 3 options for antiretroviral therapy for the patient:

- Continue taking PrEP medications.
- add a third drug to provide PEP for 28 days;
- stop taking PrEP for 1 to 2 weeks.

For patients receiving CAB injections for PrEP, as long as HIV status is confirmed, doctors should not administer a new CAB injection. During the 1 to 2 weeks required for additional HIV testing to determine HIV status, the CAB is likely to remain at a protective level.

If it is conclusively established that a patient has contracted HIV, ART should be started immediately.

If it is determined that he is not infected with HIV, CAB injections should be resumed every two months.

Side effects management:

(<10%) patients who are prescribed TDF, FTC/TDF , or FTC/TAF experience "start-up syndrome" that usually resolves within the first month of taking PrEP:

- headache *(simple analgesics / nonsteroidal anti-inflammatory drugs (NSAIDs))),*
- back pain ,
- abdominal pain ,
- weakness
- nausea or abdominal discomfort *(diet, ginger, peppermint, domperidone, metoclopramide)*
- vomit
- diarrhea *(diet, antidiarrheal drugs),*
- rash *(antihistamines)*

In case of these temporary side effects, the use of over-the-counter medications is recommended.

- Weight gain is a side effect of FTC/TAF.

Decreased kidney function is also a potential safety concernwhen using TDF, FTC/TDF, or FTC/TAF as PrEP.

- Anyone with an eCrCl ≥60 mL/min can safely be given PrEP with TDF, FTC/TDF.
- PrEP with FTC/TAF can be safely given to people with an eCrCl <60 mL/min, but ≥ 30 ml / min.

Dose adjustment in patients with altered creatinine clearance:
QC (ml / min) ≥ 50 - the recommended interval between doses every 24 hours QC (ml / min) <30-49 - the recommended interval between doses every 48 hours

Changes in the ART regimen in the development of intolerance to ARVs

Table 8 presents options for replacing antiretroviral drugs with the development of undesirable effects.

The strategy for changing regimens for patients with virologic suppression is presented in Appendix 5 to the Protocol.

The side effects of ARVs are presented in Annex 6 to the Protocol. Prescribing ARVs to patients with difficulty swallowing is presented in Appendix 7 to the Protocol.

Modification of ARVP dosages in case of impaired liver function is presented in Appendix 8 to the Protocol.

Table 8. Change of ARV drugs in the development of drug intolerance

Initial preparation	Toxic reaction	An alternative drug (in in order of priority)

AZT (ZDV)	Anemia, neutropenia, asthenia, insomnia, headache, nausea	ABC, TDF
TDF	Nephropathy, disorder bone mineralization	ABC, AZT(ZDV), DTG
ABC	Reaction Hypersensitivity	TDF, AZT(ZDV)
LPV/r	Diarrhoea	DRV/r, DRV/c, NNRTIs or DTG, RAL
	Disorders of lipid and carbohydrate metabolism	
EFV	Hepatotoxicity	DRV/r, DRV/c, LPV/ r, ETV or DTG, RAL
	Rash, erythema multiforme, fever	LPV/r, ETV, DRV/r, DRV/s or DTG, RAL
	Psychiatric disorders	ETV, LPV/r, DRV/ r, DRV /s, or DTG, RAL

Change in ART regimen with the **development of drug resistance to ARVP:** Treatment failure is defined as a continuously detectable viral load greater than 50 copies/mL based on two consecutive viral load measurements taken 2-4 weeks apart, but not earlier than six months after initiation Antiretroviral drugs. In case of treatment failure, it is necessary to conduct a study on HIV drug resistance to ARVs with a level of adherence ≥95% and a viral load level of more than 500 copies / ml.

Table 9. Second-line antiretroviral therapy regimens.

Failure of first-line therapy	**Preferred second-row schemes**	**Alternate second-row schemes**
3TC (or FTC) + TDF (or ABC) + DTG	3TC + AZT + ATV/r (or LPV/r)	3TC + AZT (or ABC) +DRV/c or ETV
3TC (or FTC) + TDF + EFV	3TC + AZT (or ABC) + DTG	3TC + AZT (or ABC) + ATV/r (or LPV/r or DRV/c or ETV)
3TC (or FTC) + TDF + RPV	3TC (or FTC) + TDF + DTG	3TC (or FTC) + TDF+ ATV/r (or LPV/r or DRV/c or ETV)

Third-line antiretroviral therapy regimens **.**

- DRV/r or DRV/s + DTG (or RAL) ± 1-2 NRTIs
- DRV/r or DRV/c + 2NRTI ± NNRTIs
- DTG+RPV

Optimization of the scheme using the genotypic profile.

A strategy for changing regimens for patients with virological failure is presented in Appendix 9 to the Protocol.

List of additional medicines :

- sulfamethoxazole and trimethoprim 480 mg;
- isoniazid 300 mg;
- azithromycin 500 mg;
- fluconazole 150 mg;
- acetylcysteine 600 mg;
- valganciclovir 450 mg;
- acyclovir 400 mg;
- pyrimethamine 25 mg;
- pyridoxine hydrochloride, 100 mg;
- rifampicin 150 mg;
- *rifabutin 150 mg;
- *rifapentine 150 mg.

**after registration in* the *territory of* the *Republic of Kazakhstan.*

Table 10: **Comparison of antiretroviral drugs:**

Class	INN	Advantages	Disadvantages	UD*
Nucleosi Bottom Ingibito Ry Back Transkri Ptaz (NRTI)	Abacavir	Nucleoside analogue, inhibiting the inverse HIV transcriptase and selectively inhibiting HIV replication 1 and HIV-2, including strains HIV-1 resistant to zidovudine, lamivudine, nevirapine. HIV resistance to abacavir in vitro and invivo It is formed slowly. Cross-tolerance to abacavir and PI HIV or NNRTIs are unlikely.	Reaction hypersensitivity to abacavir; Liver lung insufficiency , moderate to severe (classes A, B and C on the scale Child-Pugh), in connection with lack of clinical data and recommended dosage regimen; Safety of use abacavira in women in gestational time up to Not the present tense Have.	And
	Zidovudine	Active against the virus hepatitis B and Epstein virus-Barr invitro. It was found that low concentrations of zidovudine In vitro also inhibit many strains of Enterobacteriaceae, including strains of different species Shigella, Salmonella, Klebsiella,	Permanent Laboratory control of blood counts and hemoglobin in connection the possibility of development severe forms of anemia.	And

		Enterobacter and Citrobacter, as well as Escherichiacoli (while bacteria rapidly develop resistance to zidovudine). In vitro activity against Pseudomonas aeruginosa has not been established. In very high concentrations (1.9 μg/ml) inhibits Giardia lamblia, although in relation to other protozoa activity Missing.		
	Lamivudine	Active against strains HIV resistant to zidovudine. Lamivudine has an additive or synergistic effect with respect to other antiretroviral drugs, primarily zidovudine, inhibiting HIV replication in cell culture. Combination therapy with lamivudine and zidovudine in patients who have not previously received antiretroviral therapy delays the appearance of zidovudine-resistant HIV strains. Treatment of viral hepatitis B.	High incidence of cases the absence of a virological response and the occurrence of resistance at an early stage with the co-administration of lamivudine with tenofovir disoproxil fumarate and abacavir, as well as with tenofovir disoproxil fumarate in the dosage regimen 1 time per day.	And
	Tenofovir	Effective for several varieties of HIV that have resistance to AZT (ZDV). Treatment of viral hepatitis B. Prophylactic against HIV infection. It is used for Pregnancy. A single dose per day.	Renal insufficiency; careful monitoring of kidney function; osteoporosis with long-term use.	And
	Tenofovir alafenamide	It is effective for several types of HIV as part of combination therapy. Treatment of viral hepatitis B.	Increased blood levels of lactic acid	And
	Efavirenz	Adverse events by half lower than with nevirapine. Preferred NNRTIs for HIV and TB. Suitable for use in pregnant women. A single dose in day.	Persistent toxic effect on the central nervous system, mental disorders (depression, suicide risk, sleep disorders).	And
	Etravirine	High genetic barrier to development of sustainability. Use in patients with resistance to	Severe skin reactions, hypersensitivity reaction.	And

		non-nucleoside reverse transcriptase inhibitors, with experience with ART. Rapid and significant reduction in viral load in both HIV-1-infected patients who started treatment for the first time and previously treated patients with resistance to NNRTIs. Improved safety profile (effects on mental function, rash, effect on the liver and lipid profile).		
	Rilpivirine	The mechanism of action of the drug is the non-competitive inhibition of the HIV-1 virus enzyme - reverse transcriptase. Rilpivirine is an active lawsuit against human immunodeficiency virus type I. During clinical trials, rilpivirine has been shown to have a lower incidence of side effects and the same efficacy against the HIV-1 virus compared to Another non-nucleoside reverse transcriptase inhibitor is efavirenz.	There may be skin rashes, nausea, vomiting, loss of appetite, abdominal pain, headache, sleep disturbance, drowsiness , unusual dreams, dizziness , decreased mood, lipodystrophy. It has an insufficient profile of virological activity, which makes it difficult to use it with a high viral load. Contraindicated in case of hypersensitivity to the drug, with lactose intolerance, with severe hepatic insufficiency. The drug is not used in persons under the age of 18 years. It is not used during pregnancy and lactation. The drug is not used in conjunctionwith with rifampicin, anti-road drugs, glucocorticosteroids hormones of the systemic actions, proton pump inhibitors,	And
Protease inhibition	Lopinavir/ritonavir	Effectively inhibits the reproduction of the virus, it develops less often than other protease inhibitors Sustainability, good	Diarrhea, flatulence, dyslipoproteinemia. A large number of tablets to take daily dose (4).	And

		portability. Women who received therapy based on enhanced lopinavir had higher rates of immune recovery status at the time of delivery.		
	Darunavir	Improved safety and tolerability profile, high genetic barrier, including to cross-resistance. It can be used for a long time, maintaining high efficiency even with poor adherence to therapy. Approved for use in pregnantwomen. It is the optimal drug of choice in the treatment of patients with co-infection	Rash, nephrolithiasis, dyslipidemia.	And
	Atazanavir	The drug is characterized by a low incidence of resistance (about 2%), a special resistance profile (I50L mutation) and the absence of cross-resistance in most cases with other individual entrepreneurs. Distinctive pharmacokinetic features are high bioavailability and the possibility of a singledose per day	Causes a very high level of bilirubin in more than 30% of patients, a change in heart rhythm	And
Integrase inhibition	Raltegravir	It has potent antiretroviral activity, a faster decrease in viral load compared to efavirenz, at 24 and 48 weeks of treatment, and demonstrates a more rapid decrease in RNA levels of HIV-1 below the detection threshold. After 24 and 48 weeks of treatment, raltegravir did not cause an increase withserum levels of total cholesterol, low-density lipoprotein, or Triglycerides.	Nausea, increased CK.	And
	Dolutegravir	The only 2nd generation HIV integrase inhibitor with a unique resistance profile. Ease of use: 1 time per	Disorders of the nervous system. Very often: headache, dizziness, unusual dreams, insomnia.	And

		day at a dosage of 50 mg without connection with the intake of liquid, food and its composition, which allows you to maintain high adherence to treatment for a long time. High efficacy in patients with and without ART experience. Faster virological response by week 8, compared with otherdrugs. Regimens with DTG are statistically superior in efficacy to regimens with RAL in patients with resistance to at least 2 classes of ARVs. Good tolerability with a low frequency of interruption of therapy. Low interdrug rate interactions.	Gastrointestinal disorders: nausea, diarrhea, vomiting, flatulence, pain in the upper abdomen.	
	Biktegravir	Studies of the resistance profile of the drug have shown high activity against both wild-type HIV and types resistant to drugs from the NRTI classes, NNRTIs and HIV protease inhibitors. The new drug turned out to be more resistant to powerfulmutations of resistance to AI, superior to dolutegravir, and even more so raltegravir and elvitegravir.	Increased risk of obesity	In
	Cabotegravir	CAB-DD is a long-acting intramuscular drug for PrEP, the first 2 injections of which are administered at intervals of 4 weeks, and then every 8 weeks .	Requires special low-temperature storage conditions, can not be used with combined HIV/TB infections, the risk of developing mutational viral resistance to components of the drug.	In

3.3 Surgery : none.

3.4 Further management:

- Dispensary observation of patients is carried out with the written consent of the patient who has undergone consultation, examination, examination. If the identified or arrived HIV-positive patient is a foreign citizen temporarily residing in the territory of the Republic of Kazakhstan,

consultation, examination, preliminary diagnosis is made, departure to the place of citizenship is offered to receive a full range of medical services;

- removal from the dispensary registration of the patient is carried out when: the patient's death, departure to another region or country, written or collectively certified refusal of dispensary observation, failure to appear for medical examination for more than 12 months from the date of the last OSM OTRA (subject to measures toattract the patient to dispensary observation, documented), a foreign citizen temporarily residing in the territory of the Republic of Kazakhstan (subject to the implementation of all measures, listed above);
- removal from the dispensary registration of a patient receiving ART, who has left for another region of the Republic of Kazakhstan, is carried out upon confirmation of the arrival of this patient at the territorial AIDS center at the place of departure and registration for D;
- dispensary observation of patients receiving ART is carried outjointly by primary health care and territorial health organizations operating in the field of HIV prevention with a frequency of visits at least 1 time in 3-6 months. A stable patient is a patient who has been receiving ART for 1 year or more, who does not have side and toxic effects that require constant monitoring of the condition, who does not have concomitant and opportunistic diseases, pregnancy, does not breastfeed, is well aware of the need for adherence to treatment throughout lifeand has evidence of treatment success (VN analysis with two consecutive measurements ≤50 copies / ml). Dispensary examination of stable patients is carried out at least 1 time in 12 months, regardless of the stage of HIV infection. Unstable patients are examined At least 1 time in 3 months; upon reaching virological efficacy 1 time in 6 months;
- laboratory monitoring of the patient on ART;
- VN and CD4 lymphocyte counts are used to evaluate ART results;
- viral load is determined by placing thepatient on dispensary registration once or before the start of ART. In the future, VN should be measured for the first time no later than 3 months from the start of ART, then every 3 months until an undetectable level of viral load is reached, when an undetectable level of VN is reached - 1 time in 6 months, for stable patients 1 time in 12 months;
- in the absence of a decrease in VN after 6 months from the start of treatment by 1 $\log^{10}$ or a sequential twofold increase in VN after the initial suppression, a molecular genetic test should be performed to determine HIV resistance to antiretroviral drugs;

- the number of CD4 lymphocytes should be measured every 6 months, if necessary more often, then when the level of CD4≥350 cells / μl is reached, at least 1 time per year;
- laboratory studies (UAC, OAM, BAC) should be carried out at least once every 6 months, for stable patients 1 time per year;
- testing for carriage of the HLA-B allele * 5701 ** before prescribing ART regimens containing abacavir once in the presence of tests.

Table 11. Timing of laboratory tests at the beginning of ART

	Time					
	Before starting treatmen t		4 weeks	12 weeks	24 weeks	48 weeks
Viral load	X			X	X	X
CD4 lymphocyte count	X			X	X	X
Complete blood count	X		X	X	X	X
Biochemical Liver function indicators	X		X	X	X	X
Cholesterol Triglycerides	X					X
Biochemical parameters Renal function	X		x (TDF)	X	X	X

X - laboratory research is indicated regardless of the ARVs used;
x - (ARV drug) - the study is indicated for patients who receive the drug indicated in parentheses.
For patients with chronic hepatitis, biochemical parameters are determined according to the clinical protocol for the diagnosis and treatment of chronic viral hepatiB and C in adults in the Republic of Kazakhstan.

Commitment Assessment :
HV monitoring;
accounting for the dispensing of medicines; self-
reports;
calculation of the number of tablets according to the formula: (A + B - C) / Dx 100 *, where A is the number of tablets issued on the previous visit B is the balance of the ARVP on the date of the last visit in tablets
C – the remainder of the ARVP tablets for the current visit
D is the amount of ARVP that the patient should have drunk since the previous visit to thecurrent moment.

*Adherence calculation is carried out separately for each drug before each ARVP issuance.

Activities to increase commitment:

- peer counseling, nursing patronage, psychologist counseling, patient school;
- Enhanced counseling on adherence by a psychologist \Therapist;
- text messages on a mobile phone, use of mobile applications;
- the use of pill boxes;
- cognitive-behavioral therapy;
- behavioral skills training to increase commitment;
- optimization of treatment regimens with fixed-dosage drugs with medication once a day;
- multidisciplinary management;
- The principle of H = H should be discussed with all PLHIV, when making a diagnosis and at the beginning of ART / changing the ART regimen. There is now clear evidence that people living with HIV with undetectable VN do not transmit HIV sexually. In recent years, large-scale studies have been conducted on sexual transmission of HIV infection among sero-discordant couples (one partner is HIV-positive, the other is HIV-negative). In these studies, there were no cases of sexually related HIV transmission from PLHIV with undetectable HIV negative in a partner. However, a person can only find out if he or she has a suppressed viral load by taking a BH test.

Secondary prevention of relapses and complications:

- prophylaxis with Sulfamethoxazole + Trimethoprim is prescribed to all patients with CD4≤200 cells / μL for the prevention of Pneumocystis pneumonia and toxoplasmosis (800/160 mg 3 times a week); all patients with active TB, regardless of CD4 cell count, 800/160 mg daily. Prophylaxis may be discontinued in clinically stable patients with signs of immune recovery (CD4>200 μL/μL) or completion of TB treatment;
- tuberculosis (with the exception of active tuberculosis in the patient) - twiceprophylactic treatment with isoniazid (5 mg / kg), but not more than 0.3 g per day + pyridoxine at a dose of 25 mg / day for 6 months;
- At high risk of latent infection with MDR/XDR-TB :

- rifampicin 600 mg/day or rifabutin for 4 months;

- rifampicin 600 mg / day or rifabutin + isoniazid (5 mg / kg), but not more than 0.3 g per day + pyridoxine at a dose of 25 mg / day for 3 months;
- rifampicin 600 mg*2/week + isoniazid 900 mg*2/week + pyridoxine 300 mg/week for 3 months;
- rifampetin 900 mg/week + isoniazid 900 mg/week for 3 months;
- rifampetin 450 mg (<45 kg) or 600 mg (>45 kg)/day + isoniazid 300 mg/day + pyridoxine at a dose of 25 mg / day for 4 weeks;

- infection caused by MAC - in the case of CD4 <50 cells / μl - azithromycin (1250 mg 1 time per week). Cancel prophylaxis if the patient's CD4 lymphocyte count consistently exceeds 50 cells / μl for more than 3 months, resume when the number of CD4 lymphocytes drops <50 cells / μl;
- fungal infections in the case of CD4 <50 cells / μL - fluconazole (150 mg 1 time per week). Cancel prophylaxis if the patient's CD4 lymphocyte count consistently exceeds 50 cells / μl for more than 3 months, resume when the number of CD4 lymphocytes drops <50 cells / μl;
- Prevention of cryptococcosis, hystoplasmosis and coccidioidosis: the indication is profound immunodeficiency. The drugs of choice are fluconazole, 3-6 mg/kg orally daily, itraconazole, 2-5 mg/kg orally every 12 to 24 hours.

Prevention of opportunistic infections is presented in Appendix 10 to the Prevention of OpportunisticInfections.
Prevention, treatment and secondary prevention/maintenance of selected opportunistic infections are presented in Annex 11 to the Protocol.

3.5 Indicators of treatment effectiveness :

Table 12. Criteria for the effectiveness of treatment

	Virological		**Immunological**	**Clinical**	
Display l	**Viral load**		**CD4** Count	**Clinical stage**	**Portability**
Timeline[a]	24 weeks	48 weeks onwards	24 - 48 weeks onwards	12 weeks after starting ART Clinical manifestations should be absent	Continuous evaluation
Objective[b]	Less than 50 copies/mL	Less than 50 copies/mL	Increase from baseline by at least 50 cells/μL	Stage 1 or 2 Absence of clinical and subclinical manifestations HIV infection	3 months after the start of taking ARVs, the drugs are clinically manifested: Side effects

					must be absent (and subclinical, which may occur over time clinically)

a Assessment time after initiation of ART is approximate.
b Viral load decreases gradually: in most patients (except those with an initially high viral load), after 24 weeks of ART, it should be ≤50 copies/mL, or show a pronounced tendency to decrease to this level.

Divergence between virological and immunological response:

If there is a discrepancy between virological and immunological indicators, priority is given tovirological.

Laboratory monitoring:

- the number of CD4 lymphocytes should be determined every 3-6 months , to stabilize CD4 lymphocytes against the background of ART - 1 time in 12 months;
- The goal of ART is to reduce VN to an undetectable level (threshold level <50 copies of HIV RNA in 1 ml of plasma). VN is determined before the start of ART, then through

3 months after the start of treatment, with a stable virological response, the frequency of examination is at least 1 time in 12 months.

Contraception for women of childbearing age:

Women of childbearing age living with HIV should be offered contraceptive counselling.

Categories of MCP for determining the acceptability of the **use of** counter-injectives	
1	A state for which there are no usage restrictions
2	A condition in which the expected benefit of using this method Contraception generally outweighs theoretical or proven risks.
3	A condition in which the theoretical or proven risks generally outweigh the expected benefits of using this method Contraception.
4	A condition that carries an unacceptable healthrisk in using this method

Recommendations for the use of hormonal contraception in women with asymptomatic or moderate clinical course of HIV disease (stage 1 or 2)

Women with asymptomatic or moderate clinical HIV disease (stage 1 or 2) canuse the following methods of hormonal contraception without restriction: COCs, combined injectable contraceptives, combined contraceptive patches and rings, progestin-only pills, progestin-only injectables (DMPA and NET-EN), and and mplants containing levonorgestrel (LNG) and etonogestrel (ETG) (MCP, category 1).

Women with asymptomatic or moderate clinical HIV disease (stage 1 or 2) are generally able to use the LNG-IUD (MCP, category 2).

Because there may be interactions between certain hormonal contraceptive methods and some ARVs, refer to the recommendations for ART based on drug interactions.

Recommendations for the use of hormonal contraception in women with severe or progressive clinical course of HIV disease (stages 3 or 4)

Women with severe or progressive clinical course of HIV disease (stages 3 or 4) canuse the following methods of hormonal contraception without restriction: COCs, combined injectable contraceptives, combined contraceptive patches and rings, progestin-only pills, progestin-only contraceptive injectables (DMPA and NET-EN), and implants, containing levonorgestrel (LNG) and etonogestrel (ETG) (MCP, category 1).

Women with severe or progressive HIV disease (stage 3 or 4) should generally not start using the LNG-IUD (MCP, Gate 3 for initiation) until improvement occurs their conditions with the transition of the disease to an asymptomatic or moderate stage (stage 1 or 2). However, if women with an existing LNG-IUD develop severe or progressive clinical course of HIV disease, removal of the intrauterine device is not required (MCP, category 2 for continuation). Among women with an established LNG-IUD who have severe or progressive clinical course of HIV disease, the occurrence of pelvic infections should be closely monitored.

Because there may be interactions between certain hormonal contraceptive methods and some ARVs, refer to the recommendations for ART based on drug interactions.

Recommendations for women living with HIV who are receivingantiretroviral therapy (ART)

Women receiving nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) can use all hormonal contraceptive methods without restriction: COCs, combined contraceptive patches and rings, combined injectable contraceptives, NPT, progestin-only injectables (DMPA and NET-EN) and LNG and ETG implants (MCP, category 1).
Women receiving antiretroviral therapy, which includes efavirenz or nevirapine, as a rule,can use COCs, patches, rings, combined injectable contraceptives, NPT, NET-EN and implants (MCP, category 2). However, women taking efavirenz or nevirapine can use DMPA (MCP, category 1) without restriction.
Women receiving newer non-nucleoside/nucleotide reverse transcriptase inhibitors (NNRTIs) etravirine or rilpivirine can use all hormonal contraceptive methods without restriction (MCP, category 1).
Women receiving protease inhibitors (naprimer, ritonavir and ritonavir-enhanced ARVs) can generally use COCs, patches, rings, combined injectable contraceptives, PPT, NET-EN and LNG and ETG implants (MCP, category 2), and use DMPA (MCP, category 1) without restriction.
Women receiving an integrase inhibitor can use all methods of hormonal contraception without restriction (MCP, category 1).
Women receiving ARVs can use the LNG IUD (MCP, category 2) in most cases, provided that the clinical course of their HIV disease is asymptomatic or moderate (stage 1 or 2). Women with severe or progressive clinical HIV disease (stage 3 or 4) should generally not start using the LNG-IUD (MCP, category 3 for initiation) until until their condition improves with the transition to asymptomatic or moderate stage of HIV disease. However, women with an existing LNG-IUD who have developed a severe or progressive clinical course for HIV do not need to have their IUD removed (MCP, category 2 for continuation). In women with severe progressive clinical course of HIV disease, who LNG-IUDs are used, it is necessary to carefully monitor the occurrence of pelvic infections.
Management of patients with dysliepidemia is presented in Appendix 12 to the Protocol. Diagnosis and detection of bone disease in Annex 13 to the Protocol. Diagnosis and treatment of HIV-associated kidney disease in Annex 14 to the Protocol.
Diagnosis, prevention and treatment of hyperlactatemia and lactic acidosis in Annex 15 to the Protocol.

Sexual and reproductive health of women and men living with HIV in annex 16 to the Protocol.
Detection, diagnosis and treatment of depression in Annex 17 to the Protocol. Prevention of cardiovascular diseases in annex 18 to the Protocol.

IV. INDICATIONS FOR HOSPITALIZATION WITH AN INDICATION OF THE TYPE OF HOSPITALIZATION:

4.1 Indications for planned hospitalization: none.

4.2 Indications for emergency hospitalization:

- severe course of opportunistic, other secondary and concomitant diseases;
- immune reconstitution syndrome (inflammatorysyndrome of restoration of immunity - VSVI);
- adverse events on taking ARVs, 3, 4 degrees of severity: III degree (severe) - daily life is significantly impaired, often requires additional help from loved ones, medical care and treatment, possibly in a hospital;
- IV degree (extremely heavy,life-threatening) - normal daily life is impossible, requires constant help from outsiders, serious treatment, most often in a hospital.

V. TREATMENT TACTICS AT THE INPATIENT LEVEL [4 - 28]:

Treatment tactics:

- severe conditions at stages 3-4 of HIV infection;
- severe conditions in concomitant secondary diseases according to the profile of nosology.

5.1 Patient observation map, patient routing: according to the profile of nosology.

5.2 Non-drug treatment:

The regimen and diet for HIV infection depends on the defeat of individual systems and organs.

5.3 Drug treatment: see paragraph 3.2

5.4 Surgical interventions: depending on the nosology associated with hospitalization.

5.5 Further reference: see paragraph 3.4

5.6 Indicators of treatment effectiveness : see paragraph 3.5

6. ORGANIZATIONAL ASPECTS OF THE PROTOCOL:

6.1 LIST OF PROTOCOL DEVELOPERS:

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6.2 Conflict of interest: none.

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6.4 Conditions for the revision of the protocol: 5 years after its publication and from the date of its entry into force, or if new methods are available and the level of evidence.

6.5 References:

1. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach, 2021 WHO.
2. European AIDS Cinical Society (EACS*) Guidelines. Version 11.0. 2021;
3. Hormonal contraceptive methods for women at high risk of HIV and women living with HIV WHO/RHR/14.24
4. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2021, Update Clinical Practice Guideline, VTS.
5. ECDC TECHNICAL GUIDANCE HIV Pre-Exposure Prophylaxis in the EU/EEA and the UK: implementation, standards and monitoring Operational guidance, 2021
6. What's the 2+1+1? Event-driven oral pre-exposure prophylaxis to prevent HIV for men who have sex with men: update to WHO's recommendation on oral PREP. Technical brief (2019).

Annex 1

Diagnosis of cognitive disorders (neurocognitive disorders)

It is advisable to assess cognitive impairment (cognitive functions) in all HIV-infected patients without aggravating factors (severe psychiatric illness, substance abuse, including alcohol, current opportunistic infections of the central nervous system, other neurological diseases) within 6 months from the time of diagnosis. This approach allows you to accurately determine the initial indicators and, accordingly, more accurately assess the given changes. For early screening of cognitive functions, it is necessary to ask the patient 3 questions (S. Simionietal, AIDS 2009, EACS 2012): 1. Do you often have cases of memory loss (for example, you forget significant events, even the most recent, scheduledappointments, etc.)? 2. Do you feel that you have become slower to think, make plans, solve problems? 3. Do you find it difficult to focus (e.g., on a conversation, on a book, on a movie)? For each question, the patient can give one of the following answers: a) never, b) rarely, c) definitely yes. It is considered that the patient has a pathology if he answered "definitely yes" to at least one question. If a pathology is detected, if possible, it is necessary to conduct a neuropsychological examination of the patient. Neuropsychological examination should include tests to study the following characteristics of cognitive activity: auditory and visual memory, counting, speed of perception of information, attention, motor skills. (Antinorietal, Neurology, 2007).

If a pathology is detected, the patient should be examined by a neurologist, an MRI of the brain and a cerebrospinal fluid (CSF) examination for viral load and, if there are indications, a study of genotypic resistance should be carried out to drugs in a double sample of CSF and blood plasma. If the patient has a pathology of neurocognitive functions at the stage of screening or during further neuropsychologicalfollow-up, it is necessary to consider the possibility of including drugs that potentially affect the central nervous system in the regimen. These include either those drugs whose penetration into the CSF has been demonstrated in studies conducted in the treatment of the patient. HIV-infected patients (concentrations above IC90 in more than 90% of patients) or those for whom short-term (3-6 months) efficacy on cognitive function or on reducing VN on CSF has been proven, provided that the assessment is carried out in the absence of any others co-administered drugs or in controlled trials whose results are peer-reviewed (EACS 2012).

Appendix 2

Examination of HIV-infected patients in the initial and subsequent Visits

	Evaluation	At the time of formulation and diagnosis HIV	Before you begin ART	Frequency of observations	Notes
ANAMNESIS					
Medical	Complete medical history, in including :	+	+	First visit	When transferring the patient to another doctor, repeat the examination

	Family history (including early CVD, diabetes, hypertension, chronic kidney disease, liver)	+		First visit	Early CVD: cardiovascular disorders in first-degree relatives (men younger than 55 years and women younger than 65 years)
	Concomitant drug Therapy(i)	+	+	Every visit	
	Past и Current Comorbidities	+	+	Every visit	
	Vaccination history	+		Annually	Determine the antibody titer and vaccinate, in case of indications, Vaccination
Psychosocial	Lifestyle (alcohol consumption, smoking, nutrition, physical activity, drug use)	+	+	Every 6-12 months	With an unfavorable lifestyle and the presence of bad habits, more frequent observation is required Advise and provide support if necessary Advise if necessary
	Labour activity	+	+	Every visit	
	Social and domestic provision	+	+		
	Psychological Disease	+	+		
	Partner and children	+			Conduct testing of the partner and children, if they At risk
Sexual and reproductive health	Sexual history Life	+		Every 6-12 months	Take measures to address problems related to sexual dysfunction If there is a risk of transmission sexually, then it should be eliminated
	Safe sex	+			
	Partner Status and Disclosure Status	+			Consider initiating ART in HIV-discordant couples
	Problems of conception	+	+		
	Hypogonadism (including menopause)	+	+	According to Indications	Patients complaining of Sexual dysfunction
HIV INFECTION					
Virology	Confirmation of a positive test result for antibodies to HIV	+		Every 3-6 months in case of virological failure	More frequent follow-up of HIV VN at the beginning of ART. Perform a genotypic resistance test if the treatment is being carried out

	VN HIV in plasma Blood	+	+		ineffective, or if There is a risk of superinfection.
	R5-tropism (if available)		+/-		Screening, if the treatment regimen provides R5-tropic virus antagonist
Immunology	CD4: absolute count, CD4/CD8 ratio and % (you can also: CD8 and %)	+	+	Every 6 - 12 months	Annually at steady state on ART and if the CD4 count > 350 cells/µl (ii) CD4/CD8 ratio is a prognostic factor development of serious diseases
	HLA B*5701 (if available)		+		Before starting ART with ABC conduct screening if it has not been previously carried out
CO-INFECTIONS					
STIS	Serological test for syphilis	+		Yearly/ According to Indications	Screening is more frequent when there is a risk
	STI screening	+		Yearly/ According to Indications	Screening at risk and during pregnancy
Viral hepatitis	Serologic test for VHA	+		Annually/ According to indications	If there is a risk (e.g., MSM), screening , in the absence of immunity Vaccinate
	HCV screening	+			Annual screening if risk remains (e.g., MSM, IDU). Determine HCV RNA levels if HCV antibody test positive or suspected acute Infection.
	Screening for HBV	+	+		Annual screening for susceptible patients; In the absence of immunity, vaccinate. Use ART with TDF or TAF in patients who do not respond to Vaccination
Tuberculosis	G-Xpert	+	+	Repeat screening in case of contact	Consider regular G-Xpert for patients in populations with a high prevalence of tuberculosis. Usage of IGRA based on availability.
	IGRA for selected high-risk populations (if available)	+			

Other	Serological test for the virus chickenpox	+			Vaccinate , in case of indications
	Measles serological test/ rubella	+			Vaccinate , in case of indications
	Serological test for Toxoplasmosis	+			
	CMV serological test	+			
	Serological test for leishmania	+/-			Screening taking into account the countries of residence / country Origin
	Cryptococcal antigen screening	+			Screening for serum cryptococcal antigen if CD4 count < 100 μL/μL
	Examination for tropical parasites (incl. Serological schistosomiasis test)	+/-			Screening according to host countries / country of origin
	Influenza virus	+		Annually	For all HIV-positive people
	Human papillomavirus	+		According to Indications	Vaccinate all HIV-positive patients under the age of 26 years (up to 40 years if MSM). If Infection has been established HPV, the effectiveness of the vaccine is questionable
COMORBIDITIES					
Hematology	OAK	+	+	Every 3-6 months	
	Hemoglobinopathies	+			Carry out screening high-risk patients
	G6PD (glucose-6-phosphate dehydrogenase)	+			Screening patients with high Risk
Compositional Body composition	Body Mass Index	+	+	Annually	
Cardiovascular	Risk assessment (according to Framingham	+	+	Every 2 years	It is required for all men over 40 years of age and

Disease	scale (iii))				women over 50 years of age, not having CVD
	ELECTROCARDIOGRAM	+	+/-	According to the indications	Provide for an initial ECG, before starting to use antiretroviral drugs, in connection with which may cause conduction problems
Hypertension	Blood pressure	+	+	Annually	
Lipids	TC, HDL-c, LDL-c, TG(iv)	+	+	Annually	Repeat on an empty stomach (i.e. without consuming calories for 8 hours or more) if needed for medical Intervention
Glucose	Serum glucose	+	+	Annually	Consider an oral glucose/HbA1c tolerance test if fasting glucose levels are 5.7-6.9 mmol/L (100-125 mg/dL)
Lung diseases	Respiratory symptoms and risk factors(xii)	+	+	Annually	In case of complaints of severe shortness of breath with a preserved lung volume, echocardiography can be performed to exclude heart failure and / or pulmonary Hypertension
	Spirometry			According to the indications	Spirometry should be performed in all patients with symptoms(xii)
Liver diseases	Risk assessment(v)	+	+	Annually	
	ALT/AST, ALKALINE PHOSPHATASE, bilirubin	+	+	Every 3-6 months	More frequent follow-up before prescribing hepatotoxic drugs and during their application.
	Determination of the stage of fibrosis Liver			Every 12 months	In patients with HCV and/or HBV co-infection (e.g., FibroScan, serum

					fibrosis markers)
	Ultrasound of the liver			Every 6 months	In patients with cirrhosis of the liver and in patients with high-risk HBV co-infection HCC Development(xiii)
Kidney disease	Risk assessment(vi)	+	+	Annually	More frequent follow-up for risk factors for CKD (vi) and / or before and during administration of nephrotoxic Drugs(ix)
	oGFR (CKD-EPI)(vii)	+	+	Every 3-6 Months	
	Rinse urinalysis(viii)	+	+	Annually	Every 6 months if oGFR <60 ml / min or with a sharp decrease in oGFR (xiv). If proteinuria ≥1+ and/or oGFR <60 mL/min, measure BM/C or AM/K(viii)
Bone diseases	Blood biochemistry for the detection of bone diseases: calcium, phosphates (PO4), alkaline phosphatase	+	+	Every 6-12 months	
	Risk Assessment(X) (FRAX®(XI) for Patients Over 40 years)	+	+	Every 2 years	Consider DXA for individual patients.
Vitamin D	25(OH) vitamin D	+		According to Indications	Screening high-risk patients
Neurocognitive disorders	Screening Questionnaire	+	+	Every 2 years	Screening of all patients without aggravating factors. In case of detection of pathology or symptoms, refer to a psychotherapist for further examination.
Depression	Questionnaire	+	+	According to Indications	Screening high-risk patients
Cancer	Mammography			Once every 1-3 years	Women aged 50-70 years
	Pap smear			Once every 1-3 years	HIV-positive women over 21 years of age or in within 1 year after the onset of sexual activity
	Rectal examination and			Once every 1-3 years	MSM and patients with HPV-associated dysplasia.

	Anoscopy				
	Ultrasound and alpha-fetoprotein test			Every 6 months	In controversial cases / For patients with cirrhosis of the liver and patients with HBV co-infection at high risk of developing FCC (XIII)

I Review all drugs co-administered with ART that may interact with them or contribute to the growth of comorbidities; Interaction of ARVs with antidepressants Interaction of ARVs with antihypertensives Interaction of ARVs with analgesics

Interaction of ARVs with anticoagulants and antiplatelet agents Interaction of ARVs with antimalarial drugs

Interactions of ARVs with bronchodilators (for COPD) Interaction of ARVs with immunosuppressants (for PPO)

Interaction of ARVs with drugs for the treatment of pulmonary disease hypertension Interaction of ARVs with corticosteroids Interaction of ARVs with contraceptives

Interaction of ARVs with direct-acting antiviral drugs and www.hiv-druginteractions.org

II If you are on ART, have an undetectable HIV VN and a CD4 cell count > 350 cells/μL, perform a CD4 test once a year.

III There is a risk assessment formula developed on the basis of data from groups of HIV-infected patients (see: http://www.chip.dk/Tools). Note: If the patient is taking medications to control dyslipidemia and/or hypertension, the risk assessment should be interpreted with caution.

IV The calculation of LDL cholesterol for cases where triglyceride levels are not high can be found on the http://www.hivpv.org/.

V Among the risk factors for chronic liver disease: alcohol,viral hepatitis, obesity, diabetes, insulin resistance, hyperlipidemia, hepatotoxic drugs.

VI Risk factors for CKD: hypertension, diabetes, CVD, family history, belonging to the Negroid race, viral hepatitis, low CD4 cell count, smoking, age (older than average), concomitant therapy with nephrotoxic drugs.

VII oGFR: Use the SCD-EPI formula based on serum creatinine, sex, age, and ethnicity, as quantitative analysis of oGFR is valid at >60 mL/min. Alternatively, the abbreviated Renal Disease Diet Modification Formula (sDMPD) or the Cockcroft-Gault formula can be used. http://www.chip.dk/Tools

VIII Some experts recommend AM/K (urine albumin/creatinine) or BM/K (urine protein/creatinine) ratios as a screening test for proteinuria in all patients. AM / K mainly detects disease of the renal glomeruli.It is used for patients with diabetes. BM / C determines the total protein of urine against the background of diseases of the renal glomeruli and tubules.

IX Various models have been developed to determine the 5-year risk scale for CKD with different nephrotoxic ART preparations, taking into account both HIV-related and non-HIV-related risk factors. [6], [7]

X Classic risk factors: age (older than average), female sex, hypogonadism, family history of hip fractures, low BMI (≤19 kg/m2), vitamin D deficiency, smoking, lack of exercise, history of low-traumatic fracture, excessive alcohol consumption (>3 standard doses per day), steroid use (at least 5 mg for >3 months).

XI WHO's Fracture Risk Assessment Toolkit (FRAX®): www. shef.ac.uk/FRAX

XII Respiratory symptoms: shortness of breath, chronic cough and phlegm. Risk factors: smoking, occupation, air pollution, and body defenses, including previous PCP or TB, recurrent pneumonia, and alpha-1 antitrypsin deficiency. Diagnosis of COPD should be provided for older patients.

35 years old who have a risk factor (past or present smoking) and shortness of breath when

physical exertion, chronic cough, constant sputum, frequent "winter" bronchitis or dry wheezing.

XIII Screening for HCC is recommended for all patients with cirrhosis, regardless of cause. In patients with HBV without cirrhosis, screening for HCC should be conducted among those who have ever had chronic hepatitis (elevated transaminase) or with risk factors for HCC, including the presence of HCC in the family history, belonging to the or Negroid race, see HCC. http://www.easl.eu/research/our-contributions/ clinical-practice-guidelines. Individually, HCC screening may be omitted in patients without risk factorsand normal transaminase levels prior to HBV treatment.

XIV Defined as a 5 mL/min decrease in oGFR per year for 3 consecutive years or a confirmed 25% decrease in oGFR from baseline.

Annex 3 Assessing the

readiness of HIV-infected patients to start and continue ART

Purpose: To help patients start and/or continue ART	
Strategies for initiating ART have changed with the advent of the results of the START study [1]. It has been proven that starting ART on the day of diagnosis of HIV infection is possible and acceptable for people with HIV infection. However, an assessment of readiness to start ART is important so that an HIV-positive person can express their preference and not feel pressured to start ART immediately unless they have a clinical indication to do so. In order for ART to be successful, the patient's willingness to start it is necessary, as well as the correct use of the chosen treatment regimen for a long time. From awareness of the problem to the use of ART, the patient goes through a path of 5 stages. Understanding the stage of readiness of the patient, the doctor, using specialmethods, helps him to start and continue ART	Determine the patient's stage of readiness using the WEMS(I) technique and have a conversation with him, stimulating him to talk and asking questions that allow several answers: "I would like to talk to you about HIV treatment," <pause> "what do you think about this?" Based on the patient's answers, determine the stage of his readiness and then act accordingly (II). Immediate (same-day) initiation of ART should be seriously considered in the following situations: • In conditions of primary HIVinfection, especially if there are clinical signs and symptoms of meningoencephalitis (within a few hours). In this situation, the doctor may start ART immediately after a positive primary HIV test until confirmatory results of HIV testing, such as HIV VN, are obtained. • If an HIV-positive person wishes, start ART immediately. • When there is a risk that the patient will be "lost" from observation if ART is not prescribed on the same day.
Stages of readiness for the **start of ART**	
Unawareness: "I don't need it , I feel good." "I don't want to think about it."	Support: Show that you respect the patient's position/try to understand their beliefs about health and treatment/establish trust/provide brief information in according to the individual needs of the patient/set a date for the next visit.
Deliberation: "I'm weighing the pros and cons and I don't know what to do about it."	Support: show that it is okay to doubt / support the patient in assessing the pros and yes /assess what information the patient needs and help him find it / set a date next visit.
Preparation: "I want to start; I think the medication will allow me to live a normal life."	Support: support the patient's decision / choose the mostappropriate regimen together with the patient treatment/tell him about adherence to treatment, resistance, side effects, etc./discuss

	inclusion of treatment in the usual daily routine / assess the patient's self-confidence / Assess his self-efficacy. Ask: Are you sure that once you start treatment, you will be able to continue taking your medication as we have agreed (specify how)? Anduse the VAS 0-10(III) scale Think about the development of skills: • Medication training, possibly using an Electronic Drug Monitoring System (MEMS), e.g., using e-pill boxes; • Treatment under direct supervisionwith further training; • Use of reminders on a mobile phone, pill boxes, etc.; • Use, as necessary, aids and the involvement of other people.
Action: " I'll start ART now"	"Last check": Once the treatment plan is in place, is the patient ready to start ART , and is ART available?
Treatment: "I will continue" or "I have difficulties that have been going on for a long time" Caution: The patient may return to one of the previous stages, even from the "treatment" stage to the "unawareness" stage	Evaluation: Adherence - every3-6 months (IV) Rate adherence: Patients with good adherence: Show that you value their successes. Evaluation: The patient's own opinion on whether he can continue treatment and comply with the treatment regimen. Ask: Are you sure that in the next 3-6 months ofeggs you will take these medicines? Use the VAS 0-10(III) scale For patients with unsatisfactory adherence: Use the "reflection" method (V) when discussing problems; ask multiple-answer questions to identify incorrect beliefs. Assessment: Stages of readiness; Depending on it, support the patient Assessment: Obstacles and facilitators (VI). Set a date for your next visit and support the patient once again
There are **several barriers that can influence decision-making about initiating ART and adherence**	
Identification and **discussion** of **obstacles and facilitators**	
The following should be systematically evaluated: • Depression (VII) • Cognitive problems (VIII) • Alcohol or recreational drug abuse (IX)	• Topics for discussion: • Social Support and Status Disclosure • Health insurance, continuity of supply of drugs • Treatment-related factors
Identify, discuss and eliminate problems, involving, as far as possible, medical specialists of various profiles, patronage nurses, peer counselors.	

I WEMS: Waiting (> 3 sec.), Response, Reflection
II Patients who come to the doctor may be at different stages of readiness: unawareness, awareness, or preparation. First of all, you need to determine the stage at which the patient is, and then support him and continue to act accordingly. If you seek help late (CD4 < 350 cells/μL), ART should be started immediately. The patient needs close supervision and optimal support. Set the date of the next visit in the near future, i.e. in 1-2 Week.
III VAS is a visual analog scale with a range of 0 to 10 (0 to 10 = I can't handle it, 10 = I'm sure I can do it).
IV Recommended adherence questions : "How often have you missed HIV medications in the last 4 weeks: every day, more than 1 time per week, once a week, once every two weeks, once a month, never?" / "Have you ever missed two or more receptions in a row?".
V Mirroring: Repeating what the patient has said or expressed in an informal way (e.g., anger or frustration) WITHOUT introducing new elements through new questions or messages.
VI Adherence to long-term treatment.
VII Questionnaire PHQ-2 or PHQ-9 [5]. A meta-analysis shows a consistent association between depression andART infertility, not only in patients with clinical depression. Thus, evaluation and intervention aimed at reducing the severity of depressive symptoms is important even in the subclinical form. Ask questions: "Have you been bothered by the following problems in the course of e the last 2 weeks? 1. You didn't feel like doing anything; 2. You were in a bad mood, depressed or feeling hopeless." Answers: Never (0) / Several days (1) / More than half days (2) / Almost every day (3). If the patient has 2 or more points, ask seven follow-up questions
VIII Ask questions: "Do you feel that in everyday life you find it difficult to concentrate?" / "Do you feel like you're thinking slowly?" / "Don't you think you have memory problems?" / "Have your friends or relatives ever noticed that you have trouble concentrating or having trouble remembering?"
IX FAST Alcohol Abuse Questionnaire , Questions: How often in the past year have you drunk 6 or more doses (if a woman) or 8 or more doses (if a man) at a time?
0 = I can't do it, 10 = I'm sure I can).
Never = 0, Less than once a month = 1, Once a month = 2, Once a week = 3, Every or almost every day = 4. Stop if the answer is 0 (Never). Ask follow-up questions if the answer is 1, 2, 3, or 4
X The algorithm is adapted.

Annex 4

Start-up regimens for **adult HIV-infected patients starting ART for the first time**

A) Recommended treatment regimens **(you must choose one of the presented regimens)*,****

Treatment regimen	**Dosage**	**Precautions**	**Power Requirements**
2 NRTI + AI			
ABC/3TC/DTG(I, II)	ABC/3TC/DTG 600/300/50 mg, 1 tablet 1 p / day	Antacids containing Al/Ca/Mg or multivitamins should be taken after some time (at least 2 hours after or 6 hours before). DTG 50 mg with rifampicin to take 2 p / day.	No
TAF/FTC(III) or TDF/FTC(III) + DTG	TAF/FTC 25/200 mg, 1 tablet 1 p / day TDF/FTC 300/200 mg, 1 tablet 1 p / day + DTG 50 mg, 1 tablet 1 p / day		No

TAF/FTC/EVG/c(III) or TDF/FTC/EVG/c (III, IV)	TAF/FTC/EVG/c 10/200/150/150 mg, 1 tablet 1 r/day or TDF/FTC/EVG/C 300/200/150/150 mg, 1 tablet 1 p / day	Antacids containing Al/Ca/Mg, or multivitamins should be taken after some time (at least 2 hours after or 6 hours before).	During meals
TAF/FTC(III) or TDF/FTC(III) + RAL	TAF/FTC 25/200 mg, 1 tablet 1 p / day or TDF / FTC 300/200 mg, 1 tablet 1 p / day + RAL 400 mg, 1 tablet 2 p / day	It is not recommended to prescribe in conjunction with antacids containing Al or Mg. RAL 400 or 800 mg in combination with rifampicin take 2 p / day.	No
TAF/FTC/BIC	TAF/FTC/BIC 25/200/50 mg, 1 tablet 1 p / day	should not be used in conjunction with rifampicin and St. John's wort	No
2 NRTIs + NNRTIs			
TAF/FTC/RPV(III) or TDF/FTC/RPV(III)	TAF/FTC/RPV 25/200/25 mg, 1 tablet 1 p / day or TDF/FTC/RPV 300/200/25 mg, 1 tablet 1 p / day	Only if the CD4 count > 200 cells/μL and the HIV VN <100,000 copies/ml. PPIs are contraindicated; H2 blockers should be taken 12 hours before taking RPV or 4 hours after it.	During meals
2 NRTIs + IP/**r or IP/C**			
TAF/FTC(III) or TDF/FTC(III) + DRV/c(V) or + DRV/r(V)	TAF/FTC 10/200 mg, 1 tablet 1 p / day or TDF / FTC 300/200 mg, 1 tablet 1 p / day DRV / s 800/150 mg, 1 tablet 1 p / day or + DRV 800 mg, 1 tablet 1 p / day + RTV 100 mg, 1 tablet 1 p / day	Monitor patients with sulfonamide allergies.	During meals

B) Alternative treatment regimens **(use if none of the preferred regimens are available or feasible for any reason)**

Treatment regimen	**Dosage**	**Precautions**	**Power Requirements**
2 NRTI + AI			
ABC/3TC(I, II) + RAL	ABC/3TC 600/300 mg, 1 tablet 1 p / day + RAL 400 mg, 1 tablet 2 p / day	It is not recommended to prescribe together with antacids containing Al or Mg. RAL 400 or 800 mg in combined with	No

		rifampicin take 2 p / day.	
2 NRTIs + NNRTIs			
ABC/3TC(I, II) + EFV(VI)	ABC/3TC 600/300 mg, 1 tablet 1 p / day + EFV 600 mg, 1 tablet 1 p / day	Only if the HIV VN < 100,000 copies/ml	Before going to bed or 2 hours before dinner
TDF/FTC/EFV(III, VI)	TDF/FTC/EFV 300/200/600 mg, 1 tablet 1 p / day		
2 NRTIs + IP/r or IP/C			
TAF/FTC(III) or TDF/FTC(III) + ATV/c(VII, VIII) or + ATV/r(VII,VIII)	TAF / FTC 10/200 mg, 1 tablet 1 p / day or TDF / FTC 300/200 mg, 1 tablet 1 p / day + ATV / s 300/150 mg, 1 tablet 1 p / day or + ATV 300 mg, 1 tablet 1 p / day + RTV 1 tablet 100 mg 1 p / day		During meals
ABC/3TC (I, II) + ATV/c(VII, VIII) or + ATV/r(VII,VIII)	ABC / 3TC 600/300 mg, 1 tablet 1 p / day + ATV / c 300/150 mg, 1 tablet 1 p / day or + ATV 300 mg + RTV 1 tablet 1 p / day + 100 mg, 1 tablet 1 p / day	Only if the HIV VN < 100,000 copies/ml	During meals
ABC/3TC (I, II) + DRV/c (V) or + DRV/r (V)	ABC / 3TC 600/300 mg, 1 tablet 1 p / day + DRV / c 800/150 mg, 1 tablet 1 p / day or + DRV 800 mg, 1 tablet 1 p / day + RTV 1 tablet 100 mg 1 p / day	Monitor patients with sulfonamide allergy	During meals
Other schemes			
RAL(II) + DRV/c(V) or + DRV/r(V)	RAL 400 mg, 1 tablet 2 p / day + DRV / c 800/150 mg, 1 tablet 1 p / day or + DRV 800 mg, 1 tablet 1 p / day + RTV 100 mg, 1 tablet 1 p / day	Only if the CD4 count is >200 cells/μL and the HIV VN is <100,000 copies/ml. Joint appointment with antacids, containing Al or Mg, not recommended.	During meals

* Only those drugs that are currently licensed by the European Medicines Agency (EMA) to initiate therapy are considered (in alphabetical order).

** Generic HIV drugs are becoming more widely available and may change over time , as long as they replace the corresponding proprietary drug and do not violate the recommended fixed-dose combination.

I ABC is contraindicated if the HLA B*5701 test is positive. Even if thetest result for HLA B*5701 is negative, the patient should be consulted in case of a hypersensitivity reaction. ABC should be used with caution in patients at high risk of CVD (>20%).

II Use this combination only if the test for HBs Ag is negative.

III In some countries, TDF is labeled 245 mg rather than 300 mg to indicate the amount of the prodrug (tenofovir disoproxil). If possible, combination preparations containing TDF should be replaced with combination preparations containing TAF. When combined with drugs that inhibit P-glycoprotein, TAF With drugs that do not inhibit P-glycoprotein, TAF is prescribed at a dosage of 25 mg. Decision the use of TDF or TAF depends on the individual characteristics and availability of the drug.

There is limited data from long-term TAF studies. TAF*** should be preferred over TDF in patients with:

- established or high risk of CKD, see page. 51;
- co-administration with nephrotoxic drugs or prior TDF toxicity, see page 52;
- osteoporosis/progressive osteopenia or risk factors, see page. 48;
- history of fractures, see page. 50.

There are limited data on the use of TAF with oGFR <30 mL/min; **** Expert opinion in anticipation of clinical data.

IV TDF/FTC/EVG/c should only be used if oGFR ≥ 70 mL/min. It is not recommended to prescribe TDF/FTC/EVG/c to patients with an oGFR <90 ml / min, unless this is the preferred regimen.

V One study showed an increased risk of cardiovascular disease with the cumulative use of DRV [13].

VI EFV: do not prescribe if there is a history of suicide attempts or mental illness; are not active against HIV-2 and HIV-1 group O strains.

VII Concomitant use of PPIs is contraindicated. If co-administration with PPIs is unavoidable, consider an alternative regimen; you can increase the dose of ATV to 400 mg 1 p / day, careful clinical monitoring is recommended. It is not recommended to exceed PPI doses comparable to omeprazole 20 mg. They should be taken approximately 12 hours before ATV/r. H2 antagonists should be taken 12 hours before or 4 hours after ATV.

VIII Potential renal toxicity with ATV/r and ATV/c.

Appendix 5 Regimen

Change Strategies for Patients with Virologic Suppression

Definition of virologic suppression:

In clinical trials investigating regimen change strategies, suppression is determined by the amount of HIV VN <50 copies/mL for at least 6 months.

Indications for **changing the regimen for patients with virologic suppression**

- Documented toxicity caused by one or more ARVs included in the regimen. Examples of such toxicity include lipodystrophy (AZT), central nervous system side effects (EFV), diarrhea (PI/r) and jaundice (ATV), proximalrenal tubulopathy, and low bone mineral density (TDF).
- Prevention of long-term toxicity. An example of such a change in regimen: prevention of lipodystrophy in patients taking AZT and prevention of proximal renal tubulopathy with TDF.
- Anticipation of severe drug interactions.
- Planned pregnancy.
- Aging and/or concomitant disease with possible negative effects of drugs in the current regimen, e.g., CVD risk, metabolic parameters.
- Simplification of the scheme: Reduce the number of dosage units taken by the patient, adjust food restrictions and improve adherence.
- Initiation of HCV treatment in case of drug interactions.

Principles:

Clinicians should always consider possible side effects or tolerability issues with current antiretroviral regimens. It should not be assumed that a patient with HIV infection has adapted and tolerates the current regimen well, relying only on the hypocrisyof VN HIV.

1. The objectives of changing the treatment regimen should be to eliminate or improve adverse events, promote adequate treatment of comorbidities and improve the quality of life.

2. It is especially important when changing the scheme not to put at riskin irusological suppression. In patients with no history of virological failure and resistance, a change in treatment regimen entails a low risk of subsequent failure if clinicians choose one of the recommended first-line therapy combinations. Most In clinical trials showing no less effectiveness of the new regimen after the change, patients with previously identified virological failures were actively excluded.
3. Before any change in treatment regimen, it is necessary to analyze the patient's complete history of taking ARVs with his HIV VN indicators, tolerability issues and a cumulative genotypic study of drug resistance.
4. PI/r or PI/C can be replaced by unboosted ATV, NNRTI, or AI only if the full activity of the two NRTIs remaining in the treatment regimen can be guaranteed. The change of the scheme should be planned especially carefully if it can lead to a decrease in the genetic barrier of the scheme in the event of previous virological failures. Before changing the regimen, you should review the complete history of ART and the available test results for resistance and VN HIV and make sure that there are no drug interactions that can lead to suboptimal concentrations of drugs in the blood (for example, nebustersanT and TDF).
5. Before changing drugs, it is necessary to take into account the options for other treatment regimens in case of potential virological failure when using a new regimen. For example, the development of the M184V RT mutation in patients with HIV infection who have suffered a virologicalfailure when taking a regimen containing 3TC may exclude the use of all currently available combination drugs "the whole regimen in one tablet".
6. Changing one drug to another with the same genetic barrier (e.g., EFV to RAL) is generally considered virologically safe in the absence of resistance to the new component of the regimen.
7. Careful consideration should be given to the possibility of drug interactions with the new regimen.
8. If the change of regimen involves discontinuation of TDF and exclusion of the initiation of TAF, the patient's HBV status should be checked (avoid discontinuation of TDF in patients with chronic HBV, determine the vaccination status ofHBV).
9. Patients with HIV infection should be examined soon after changing treatment regimens (e.g., after 4 weeks) to ensure that the level of suppression is maintained and to check the regimen for possible toxicity.
10.If a patient with HIV infection is taking therapy and tolerates a regimen that is no longer the preferred option, there is no need to change the regimen. For example: the patient tolerates a regimen containing EFV well.
11.Online video lectures are available - Modifying the ART regimens of the EACS web course on HIV treatment.

Gentle strategies

Dual therapy:

- DTG + RPV
- 3TC+ (DRV/r or DRV/c) or 3TC+ (ATV/r or ATV/c)

Clinical studies have not shown that these strategies are associated with more frequent cases of relapsing viremia compared to triple therapy.

Monotherapy with DRV/r:

In clinical studies, this strategy has been associated with more frequent cases of recurrent viremia compared to triple therapy. As an exception, monotherapy with DRV/r may be an appropriate treatment option for patients who are not indicated for double therapy.

Dual therapy with 3TC + PI/r or monotherapy with DRV/r can only be given to individuals

a) who do not have resistance to PI,
b) with HIV VN suppression to < 50 copies/mL for at least the last 6 months, and
c) in the absence of co-infection with chronic HBV.

Deprecated strategies

a. Monotherapy with ATV/r
b. Monotherapy with DTG
c. Triple NRTI Combination
d. Combination of 2 drugs, e.g., 1 NRTI + 1 NNRTI, or 1 NRTI + 1 non-boosted PI, or 1 NRTI + RAL, or 2 NRTIs, MVC + RAL, IP/r or IP/c + MVC , ATV/r or ATV/c + RAL.
e. Intermittent therapy, consecutive or long interruptions in treatment (27 days or more).

Annex 6

Side effects of **ARVs (by class)**

	Skin	**Digestive tract**	**Liver**	**CCC**	**Loco motor naya System s A**	**Urine reproduc tive system**	**Nerv ous Syste m Ma**	**Fat deposit s**	**Metabo lism**	**Other**
NRTI										
ABC	Rash*	Nausea * Diarrhea *		IHD						*Systemic hypersensitiv ity syndrome (HLA*B5 701-dependent)
ZDV(ii)	Nail pygman ization	Nausea	Steatosis		Myopa tia , Rabdo Myolysis			**Lipo atro fia**	Dyslipidemia Hyperlac Tatemy	Anemia
d4T(ii)		Pancreatit it	**Steatosis**				**Peripher al neuropat hy of the neurop Tia**		**Dyslipi Demia,** Hyperlac Tatemia	
ddI(ii)			Steatosis , liver fibrosis	IHD					Hyperlactate my	
3TC										
FTC										
TDF(iii)			Hepatitis		↓ IPC, Osteo ma alation ↑ Fracture risk in	↓ oGFR, Fanconi syndrome				
TAF(III)										
NNRTIs										

EFV	Rash		Hepatitis				**Depression, sleep disorders,** headache Suicidal Thoughts		**Dyslipidemia** Gynecomastiia	**↓ 25(OH) Vitamin D**
ETV	Rash									
NVP	Rash*		Hepatitis*							* Systemic hypersensitivity (in Constraints from CD4 and floor)
RPV	Rash		Hepatitis			↓ oGFR(iv)	Depress, sleep disorders, headache			
UI										
ATV(V)			**Hyper-biliru binemi i** Jaundice a Cholelite iaz			↓ oGFR, nephrolite iaz			Dyslipi demia	
DRV(V)	Rash			IHD		Nefroli Thiaz			Dislipi Demia	
LPV		**Sickening ta Diare i**(VII)		IHD		↓ oGFR			**Dyslipi demia**	

I "Frequent side effects" (complications that may occur in at least 10% of HIV-infected patients receiving ART) are shown in bold. "Severe side effects" (complications that can be life-threatening and require immediate medical attention) are highlighted in red. "Infrequent and non-severe side effects" are represented in the usual black font.

II Currently available, but generally not recommended due to its toxicity

III Tenofovir disoproxil fumarate (TDF) is a classic inactive form of tenofovir. TAF has a lower rate of adverse reactions from the kidneys and bones associated with the use of tenofovir, but there is a lack of long-term experimental data, see pages 51-52 and page 48.

IV Due to inhibition of tubular secretion of creatinine by the kidneys without affecting the glomerular filtration itself. V ATV can be used both boosted and non-boosted by RTV or COBI in low doses.

ATV-related adverse reactions are more common with boosting. DRV can be used in boosted form with RTV or COBI in low doses. Both RTV and COBI, used in low doses as boosters, can cause similar minordigestive problems.
VI Currently available, but rarely used. Requires RTV boosting.
VII The frequency and severity differ depending on the ARV drug. viii Cases of drug syndrome have been recorded hypersensitivity (6 cases in total).

* Effects associated with a hypersensitivity reaction.

Note: The aggregate side effects presented in the above table is not exhaustive, but it presents all the most significant effects with an indication
possible causal relationship with the use of the drug. Patients receiving ART often experience nausea, diarrhoea and rash, and these symptoms are listed in the drugtable.
where possible causal relationships established on the basis of clinical observations are indicated.

Annex 7

Prescribing ARVs to **patients with difficulty swallowing**

Preparation	**Release** form	**Grind tablets**	**Open capsules**	**Notes**
NRTI				
ABC	tablets (300 mg) solution (20 mg/ml)	Yes		Bitter taste. The crushed tablets can be added to a small amount of semi-solid food or to liquids that should be consumed immediately
3TC	capsules (200 mg) solution (10 mg/ml)(vii)	Yes		The crushed tablets can be added to a small amount of semi-solid food or to a liquid, which should be consumed immediately
TDF	tablets (300(i) mg)	Yes		Better: dissolve in ≥ 1 deciliter water/juice (orange or grape), bitter taste
ZDV	capsules (250 mg)	No	No	Astringent, bitter taste
	syrup (10 mg/ml)			Better: use syrup or inject intravenously at 6 mg/kg daily in a 5% glucose solution
TAF/FTC	tablets (25/200 mg and 10/200 mg)(V)	No		It is necessary to swallow the tablet whole. The tablet should not be chewed, broken, cut, or crush
TDF/FTC	tablets (300(I)/200 mg)	Yes		Better: dissolve in ≥ 1 deciliter water/juice (orange or grape), bitter taste
ABC/3TC	tablets (600/300 mg)	No		Use a solution of separate Components
ZDV/3TC	tablets (300/150 mg)	Yes		Loosen in water (≥ 15 ml); Another option: use a solution of separate Components

ABC/3TC/ZDV	Pills (300/150/300 mg)	No		Use a solution of separate Components
NNRTIs				
EFV	tablets (600 mg)	Yes		It is difficult to dissolve; the solution has less bioavailability; If body weight > 40 kg, use a dose of 720 mg
	capsules (50, 100, 200 mg)	No	Yes	
	solution (30 mg/ml)			
ETV	tablets (200 mg)	No		Loosen in water (≥ 5 ml). Water should be added to the glass several times, each time the solution should be fully drunk to guarantee the consumption of a whole dose of the drug.
NVP	tablets (200, 400 mg(II)) suspension (10 mg/ml)	yes(ii)		Dissolve in water
RPV	tablets (25 mg)	No		Crushing tablets and adding to the liquid is not recommended. RPV is insoluble in water over a wide range pH.
TDF/FTC/EFV	Pills (300(i)/200/600 mg)	No		
TAF/FTC/RPV	tablets (25/ 200/25 mg)	No		It is necessary to swallow the pill wholly. The tablet should not be chewed, crushed or crushed
TDF/FTC/RPV	tablets (300(i)/200/25 mg)	No		Crushing tablets and adding to the liquid is not recommended. RPV insoluble in water over a wide pH range .
UI				
ATV	capsules (150, 200, 300 mg)	No	Yes	It is difficult to open; Take during Food
ATV/sec	tablets (300/150 mg)	No		It is necessary to swallow the tablet whole. The tablet should not be chewed, broken, cut, or crush
.DRV	tablets (75,150, 400, 600, 800 mg) solution (100 mg/ml)	Yes		Take with food. The crushed tablets can be added to a small amount of semi-solid food or to a liquid that should be consumed Right away
DRV/c	tablets (800/150 mg)	No		
LPV/r	tablets (200/50 mg) solution (80/20 mg/mL)	No		Alcohol 42%, do not dilute in water (precipitation may occur), drink milk (not water); Take with meals, bitter taste: dilute in milk-chocolate drink
RTV	tablets (100 mg) solution (80 mg/ml)	No		Alcohol 43%, do not dilute the solution (precipitation may occur), drink milk (not water); bitter taste; Take VO Meal Times

Other				
DTG	tablets (50 mg)	Yes		The crushed tablets can be added to a small amount of semi-solid food or to a liquid, which should be consumed immediately.
MVC	tablets (150, 300 mg)	Yes		Although the company does not possess any specific kinetic information, the grinding of the tablets does not imply a negative effect on Bioavailability
RAL(iii)	tablets (400 mg) chewable tablets (25, 100 mg)	Yes		Chewable tablets have a higher bioavailability: 300 mg chewable tablet (= 400 mg tablet in a film shell)
TAF/FTC/EVG/c	tablets (10/ 200/150/150 mg)	No		It is necessary to swallow the tablet whole. The tablet should not be chewed, broken, cut, or crush
TDF/FTC/EVG/c	tablets (300(i)/200/150/150 mg)	No		Grinding tablets has practically no effect on the pharmacokinetic Profile(iv)
ABC/3TC/DTG (vi)	tablets (600/300/50 mg)	Yes		The crushed tablets can be added to a small amount of semi-solid food or to a liquid, which should be consumed immediately
Prevention/treatment of opportunistic infections				
Azithromycin	tablets (250 mg) suspension (40 mg/ml)	No		
Cotrimoxazole	tablets (400/80, forte 800/160 mg) solution (40/8 mg per ml)	Yes; Forte is hard		Dilute the solution with water 3-5 times (high osmolality)
Fluconazole	capsules (50-200 mg) suspension (40 mg/ml)	No	Yes	
Pyrimethamine	tablets (25 mg)	Yes		Take with food
Valganciclovir	tablets (450 mg) solution (50 mg/ml)	No	No	Difficult to dissolve
Rifampicin	tablets (450, 600 mg)	Yes		Take on an empty stomach
	capsules (150, 300 mg)	No	Yes	
	suspension (20 mg/ml)			
Rifabutin	capsules (150 mg)	No	Yes	Mix with apple sauce, syrup (insoluble in water)
Isoniazid	tablets (100, 150 mg)	Yes		Take on an empty stomach
Pyrazinamide	tablets (500 mg)	Yes		

Streptomycin	tablets (100, 400 mg)	Yes		Difficult to dissolve Better: use the solution intravenously
Rifampicin/iso-Niazide	tablets (150/100, 150/75 mg)	Yes		Take on an empty stomach
Rifater (Rifampicin, Isoniazid, pyrazinamide)	tablets (120/50/300 mg)	Yes		Take on an empty stomach
Rimstar (rifampicin, isoniazid, pyrazinamide, ethambutol)	tablets (150/75/400/275 mg)	Yes		Take on an empty stomach
Ribavirin	capsules (200 mg)	No	Yes	Loosen in orange juice, Take with meals

I In some countries, TDF is labeled 245 mg rather than 300 mg, indicating the amount of the prodrug (tenofovir disoproxil) rather than the fumarate salts (tenofovir disoproxil fumarate).

II The effect of prolonged release is lost. Note: Taking NVP 400 mg 1 time per day (immediate-release) for patients with a large body weight (≥ 90 kg) may result in
minimum subtherapeutic concentrations, as when taking NVP 200 mg twice a day. Thus, for people with a large body weight, it is preferable to take NVP twice a day.

III Grinding of tablets is not recommended in the instructions for use of the drug, however, the absorption of RAL did not change when the drug was crushed, grown in 60 ml of warm water and administered through a gastrostomy tube. In addition, the absorption of RAL with 400 mg of RAL 2p / day was higher in those patients who chewed the tablets, and did not swallow them whole.

IV Grinding tablets is not recommended in the instructions for use of the drug, however, the pharmacokinetic profile of TDF / FTC / EVG / c did not change significantly after the combination drug (Stribild) was crushed and taken with a meal or in adrip infusion, compared with taking the whole tablet

V TAF is used at a dosage of 10 mg if taken concomitantly with drugs that inhibit P-glycoprotein, and at a dosage of 25 mg if taken concomitantly with drugs thatdo not show an inhibitory effect on
P-glycoprotein.

VI The pharmacokinetic profiles of DTG/ABC/3TC did not change to a clinically significant degree after the tablet with a fixed dosage (Triumeq) was crushed and added to water or enteral nutrition [14].

VII The bioavailability of 3TC solution has been shown to be significantly reduced in a dose-dependent
manner by sorbitol present in other liquid formulations (e.g., ABC, NVP, cotrimoxazole)

Annex 8

Modification of dosages of ARVs in case of **impaired liver function**

NRTI	
ABC	Child-Pugh Classification A: 200 mg 2 p / day (use a solution for P / Oh intake) Child-Pugh classification B or C: contraindicated
FTC	Without dosage adjustment
3TC	Without dosage adjustment
TAF	Without dosage adjustment

TAF/FTC	Without dosage adjustment
TDF	Without dosage adjustment
TDF/FTC	Without dosage adjustment
ZDV	Reduce the dose by 50%, or double the intervals between doses, if the classification is according to Child-Pugh C
NNRTIs	
EFV	No dosage changes; For patients with impaired liver function, use with caution.
TDF/FTC/EFV	
ETV	Child-Pugh classification A or B: no dosage correction Child-Pugh classification C: no data available
NVP	Child-Pugh classification B or C: contraindicated
RPV	Child-Pugh classification A or B: no dosage adjustment Child-Pugh classification C: no data available
TAF/FTC/RPV	Child-Pugh classification A or B: no dosage adjustment Child-Pugh classification C: no data available
TDF/FTC/RPV	Child-Pugh classification A or B: no dosage adjustment Child-Pugh classification C: no data available
UI	
ATV	Child-Pugh B classification: 300 mg 1p / day
	Child-Pugh C classification: not recommended
	Boosting with ritonavir is not recommended for patients with impaired hepatic function (Child-Pugh classification B or C)
.DRV	Child-Pugh Classification A or B: No Dosage Adjustment
	Child-Pugh C classification: not recommended
DRV/c	Child-Pugh classification A or B: no dosage adjustment
	Child-Pugh C classification: not recommended
LPV/r	No dosage recommendations; For patients with impaired liver function, use with caution.
RTV	Cm. recommendations for primary PI
MVC	No dosage recommendations. For patients with impaired hepatic function, concentrations are likely to increase
AI	
RAL	Without dosage adjustment
EVG	Child-Pugh classification A or B: no dosage adjustment Child-Pugh C classification: N/A
DTG	Child-Pugh Classification A or B: No Dosage Adjustment Child-Pugh C classification: N/A
TAF/FTC/EVG/c	Child-Pugh Classification A or B: No Dosage Adjustment Child-Pugh C classification: N/A
TDF/FTC/EVG/c	Child-Pugh Classification A or B: No Dosage Adjustment Child-Pugh C classification: N/A
ABC/3TC/	To use individual components, see Appropriate corrections

DTG	
TAF/FTC/ BIC	To use individual components, see Appropriate corrections

Note: Impaired liver function is an important indication for therapeutic observation of drugs, since the experience of correcting such dosages in clinical settings is very limited.

Annex 9

Virological failure

Definition	**INCOMPLETE SUPPRESSION**: HIV VN > 200 copies/mL 6 months (i) after initiation of therapy in patients who have not previously received ART. **VN RESUMPTION**: Confirmed HIV VN > 50 copies/mL in patients with previously undetectable HIV VN.
	Revise the expected effectiveness of the treatment regimen
	Assess patient adherence, readiness, tolerability, medication interactions and interactions of drugs with food , the psychosocial state of the patient
	Perform a test for resistance to drugs of an ineffective treatment regimen (usually performed with HIV VN > 350-500 copies / ml and in specialized laboratories at lower levels of viremia) and obtain test results for resistance from the anamnesis, to determine the initial registered mutations
	Perform a tropism test
	If possible, conduct therapeutic monitoring of drugs
	View a history of ARV treatment
	Identify possible treatment options: active and potentially active drugs/combinations
General measures	Revise the expected effectiveness of the treatment regimen
	Assess patient adherence, readiness, tolerability, medication interactions and interactions of drugs with food , the psychosocial state of the patient
	Perform a test for resistance to drugs of an ineffective treatment regimen (usually performed with HIV VN > 350-500 copies / ml and in specialized laboratories at lower levels of viremia) and obtain test results for resistance from the anamnesis, to determine the initial registered mutations
	Perform a tropism test
	If possible, conduct therapeutic monitoring of drugs
	View a history of ARV treatment
	Identify possible treatment options: active and potentially active drugs/combinations
What to do in case virological failure	**If HIV VN** > 50 **and < 500 copies/ml, then:**
	Check Commitment
	Check the level of HIV VN in blood plasma after 2-4 weeks
	If the genotype cannot be determined, then consider the possibility of changing the regimen, based on previous treatment and data on resistance in the anamnesis

	If the level of **HIV VN > 500 copies / ml is confirmed**, **then:**
	Change the treatment regimen as soon as possible. What kind of drugs to change – will depend on the results of the resistance test:
	If no resistance mutations are detected, double-check the patient's adherence,
	If resistance mutations are detected, then change the treatment regimen to suppressive, taking into account the history of treatment; Consultations with specialists in various fields are recommended
	The goal of the new treatment regimen : HIV VN < 50 copies/ mL at 6 months
If available resistance mutations	**General recommendations:**
	In the new scheme, use at least 2 or preferably 3 active drugs (including active drugs from previously used classes), based on previous resistance mutations that are present in the current or previous genotypic test
	Any regimen should include at least 1 fully active IP/r (e.g., DRV/r) plus 1 drug from a class that has not been used before, e.g., fusion inhibitor, AI, or CCR5 antagonist (if the tropism test shows the presence of only R5-t virus), or 1 NNRTIs (e.g., ETV), selected based on the results of a genotypic test
	If, based on resistance data, there are < 2 active drugs left, then postpone the changes, except in cases with low CD4 counts (< 100 cells / μL) or cases with a high risk of clinical deterioration, when the goal is to preserve the immune system functions by partially reducing the viral load (reduction > 1 * $\log_{10}$) with repeated use of ARVs
	If the options are limited, experimental ones should be considered drugs or new drugs, giving preference to participation in clinical trials (but functional monotherapy should be avoided)
	Interruption of treatment is not recommended.
	In some cases, it is possible to continue using 3TC or FTC even with a proven resistance mutation (M184V/I)
	In the presence of several variants of regimens, the criteria for the preferred selection of regimens include: simplification of the regimen, assessment of the risk of toxicity, drug interactions, potential salvage therapy
In patients with very high baseline HIV VN (> 100,000 to 500,000 copies/mL), viral load suppression may take more than 6 months	

Annex 10 Prevention

and treatment of opportunistic infections (OIs) in patients with HIV infection

Primary prevention of OI according to the **stage of immunodeficiency**

CD4 count threshold/reading
If CD4<200 cells/μL, CD4%<14% recurrent oral candidiasis or appropriate concomitant inhibition of immunity *

Prevention of Pneumocystis pneumonia (PCP) and toxoplasmosis

Stop: if CD4 > 200 cells/μL for more than 3 months or CD4 100-200 cells/μL and undetectable HIV for more than 3 months

* For example, the use of corticosteroids with the equivalent of prednisone > 20 mg for more than 2 weeks, chemotherapy, high molecular weight drugs such as rituximab and others. Decisions to start and terminate in such situations should be made individually.

	Preparation	Dose	Comments
Positive or negative Serology for toxoplasmosis	**TMP-SMX**	1 double-dosage tablet (DS) (800/160 mg) 3 x/week P/O or 1 tablet of the usual dosage (ss) (400/80 mg) 1 x / day P / O or 1 tablet DS 1 x / day P/O	
Negative serology for toxoplasmosis	**pentamidine**	300 mg in 6 ml sterilized water 1 x Inhalation/month	Does not prevent rare extrapulmonary manifestations of P. jirovecii
Negative serology for toxoplasmosis	**Dapsone**	1 x 100 mg/day P/O	G6PD Insufficiency Control
Positive or negative Serology for toxoplasmosis	**Atovaquone suspension**	1 x 1500 mg/day P/O (with food)	
Positive serology for toxoplasmosis	**Dapsone + pyrimethamine + folinic acid**	200 mg 1x/week P / O 75 mg 1x / week P / O 25 mg 1x/week P/O	G6PD Insufficiency Control
Positive serology for toxoplasmosis	**Atovaquone suspension +/- pyrimethamine + folinic acid**	1 x 1500 mg/day P/O (with food) 75 mg / week P / O 25-30 mg / week P / O	
CD4 count **< 50 cells/μL**			
Prophylaxis against nontuberculous mycobacteria (M. avium complex, M. genavense, M. kansasii) Consider prophylaxis only if there is no clinical suspicion of the spread of non-uberulic bacteria. Prophylaxis may be delayed if cART has been started within four weeks. Stop: if CD4 > 100 cells/μL for more than 3 months and the patient is on effective ART (and, according to experts, HIV is undetectable)			
Schemes recommended as alternatives	azithromycin	1 x 1200-1250 mg/ week P/O	Check for interaction with ART
	or clarithromycin	2 x 500 mg/day P/O	
	or Rifabutin	1 x 300 mg/day P/O	Check for interaction with ART

Annex 11

Primary prevention, treatment and secondary prevention/ maintenance therapy of selected OIs

Pneumocystis pneumonia (PCP)

Primary prevention			
Indications : if CD4 < 200 cells/µL, CD4% < 14% recurrent oral candidiasis or corresponding concomitant immune suppression (see above) Stop: if CD4 > 200 cells/µL for more than 3 months or CD4 100-200 cells/µL and HIV VN undetectable for more than 3 months			
	Preparation	**Dose**	**Comment**
Positive or negative Serology for toxoplasmosis	TMP-SMX	1 tablet double dosages (800/160 mg) 3 x / week P / O or 1 tablet Usual Dosages (400/80 mg) 1 x / day P / O or 1 Tablet Double Dosage 1 h/day P/O	
Negative serology for toxoplasmosis	pentamidine	300 mg in 6 ml of water 1 x Inhalation/month	Does not prevent rare extrapulmonary manifestations P. JIROVECII
Negative serology on Toxoplasmosis	Dapsone	1 x 100 mg/day P/O	Control G6PD insufficiency
Positive or negative Serology for toxoplasmosis	Atovaquone suspension	1 x 1500 mg/day P/O (with food)	
Positive serology for toxoplasmosis	Dapsone + pyrimethamine + folinic acid	200 mg 1 x/week P/O 75 mg 1 x/week P/O 25-30 mg 1 x/week P/O	G6PD Insufficiency Control
Positive serology for toxoplasmosis	Atovaquone suspension +/- pyrimethamine + folinic acid	1 x 1500 mg/day P/O (with food) 75 mg 1 x / week P / O 25-30 mg 1 x / week P / O	
Treatment			
At least 21 days, followed by secondary prophylaxis until the CD4 count > 200 cells/µL and the HIV VN is undetectable for more than 3 months. Diagnostics: - Definitive diagnosis: Cough and dyspnea on exertion AND diagnosis by cytology/histopathology ofinduced sputum (sensitivity up to 80%), bronchoalveolar lavage (sensitivity >95%) or bronchoscopic tissue biopsy (sensitivity >95%) - Preliminary diagnosis: CD4 lymphocyte count < 200 cells/µL AND shortness of breath / decreased perception with physicalexertion and cough AND PCP-compatible radiology AND no evidence of bacterial pneumonia AND response to PCP treatment.			
Preferred therapy	TMP-SMX	3 x 5 mg/kg/day TMP IV/P/O	The benefits of corticosteroids if

	+ prednisone if PaO_2 <10 kPa or <70 mmHg or alveolar/arterial gradient O_2 > 35 mmHg Start predni-zoning for 15-30 min to TMP/SMX	+ 3 x 25 mg/kg/day SMX IV/V/P/O 2 x 40 mg/day P/O 5 days 1 x 40 mg/day P/O 5 days 1 x 20 mg/day P/O 10 days	started before 72 hours after the start of treatment
Alternative therapy for moderate to severe PCP	Primakhin + clindamycin	1 x 30 mg (base)/day P/O 3 x 600-900 mg V/V/P/O	G6PD Insufficiency Control
	or pentamidine	1 x 4 mg/kg/day IV (infusion in for 60 min.)	
	For each scheme: + prednisaloone if PaO_2 <10 kPa or <70 mmHg . or alveolar/ arterial gradient O_2 > 35 mmHg Start prednisone 15-30 min before TMP/SMX. Some experts recommend the addition of caspofungin to the standard treatment of patients with PCP (necessary hospitalization and intensive care)	2 x 40 mg/day P/O 5 days 1 x 40 mg/day P/O 5 days 1 x 20 mg/day P/O 10 days	Use of corticosteroids if started before 72 hours
Alternative therapy for mild to moderate PCP	Primakhin + clindamycin	1 x 30 mg (base)/day P/O 3 x 600-900 mg/day P/O	G6PD Insufficiency Control
	or Atovaquone suspension	2 x 750 mg/day P/O (with food)	
	or Dapsone + trimethoprim	1 x 100 mg/day P/O 3 x 5 mg/kg/day O /O	Control of G6PD Insufficiency In Case of Rash: Reduce TMP Dose (50%), antihistamines

			Drugs
Secondary Prevention / Supportive Care			
Stop: if CD4 > 200 cells/µL and undetectable HIV for more than 3 months			
Positive or negative serology for toxoplasmosis	TMP-SMX	1 tablet of double dosage (800/160 mg) 3 times / week P / O or 1 tablet of normal dosage (400/80 mg) 1 time / day P / O or 1 tablet of double dosage 1 time / day P/O	
Negative serology for toxoplasmosis	pentamidine	300 mg in 6 ml of sterilized water 1 inhalation/month	Do not use in case of rare extrapulmonary manifestations of P. JIROVECII
Negative serology on Toxoplasmosis	Dapsone	1 x 100 mg/day P/O	G6PD Insufficiency Control
Positive or negative serology for toxoplasmosis	Atovaquone suspension	1 x 1500 mg/day P/O (with food)	
Positive serology for toxoplasmosis	Dapsone +/- pyrimethamine + folinic acid	200 mg 1 x / week P / O 75 mg 1 x / week P / O 25-30 mg 1 x / week P / O	G6PD Insufficiency Control

Toxoplasma encephalitis

Primary prevention			
Indications: if CD4 < 200 cells/µL, CD4%<14% recurrent oral candidiasis or corresponding concomitant immune suppression (see above) **Stop:** if CD4 > 200 cells/µL for more than 3 months or CD4 100-200 cells/µL and HIV VN undetectable for more than 3 months			
	Preparation	**Dose**	**Comments**
Preferred prophylaxis	**TMP-SMX**	1 tablet double Dosages (800/160 mg) 3 h/week P/O or 1 tablet Usual dosage (400/80 mg) 1 h/day P/O or 1 double-dosage tablet 1 h/day P/O	All of these schemes treatment also effective against PCP
Alternative prevention	**Atovaquone suspension**	1 x 1500 mg/day P/O (with food)	
	Dapsone **+ pyrimethamine** **+ folinic acid**	200 mg 1 x/week P/O 75 mg 1 x/week P/O 25-30 mg 1 x/week	G6PD Insufficiency Control

		P/O	
	Atovaquone suspension **+/- pyrimethamine** **+ folinic acid**	1 x 1500 mg/day P / O (with food) 75 mg 1x/week P/O 25-30 mg 1 x / week P / O	
Treatment			
Treat for 6 **weeks,** followed by secondary prophylaxis until the CD4 cell count > 200 cells/µL for > 6 months **Diagnosis:** - **Definitive diagnosis:** Clinical Symptoms Typical radiology Brain And cytological/histological detection **Presumptive diagnosis:** clinical symptoms, typical radiology AND response to empirical treatment. It is the standard in most clinical settings			
Preferred therapy	**pyrimethamine** **+ sulfadiazine** **+ folinic acid**	Day 1: 200 mg P/O, **then** if ≥ 60 kg; 1 x 75 mg/day P/O if < 60 kg: 1 x 50 mg/day P/O if ≥ 60 kg: 2 x 3000 mg/day/B/B if < 60 kg: 2 x 2000 mg/day/P/O/B/B 1 x 10-15 mg/day P/O	To control the myelotoxicity of pyrimethamine, the main Neutropenia Sulfadiazine is associated with crystalluria and can lead to kidney failure and urolithiasis. Good hydration is important. Check your kidney function and urine sediment for microhematuria and crystalluria.
	pyrimethamine **+ clindamycin** **+ folinic acid**	Day 1: 200 mg/day P/D, **followed by** if ≥ 60 kg: 1 x 75 mg/day P/O if < 60 kg: 1 x 50 mg/day P/O 4 x 600-900 mg/day P/B/B 1x 10-15 mg/day P/O	To control the myelotoxicity of pyrimethamine, mainly neutropenia Additional prevention of PcP is important
Alternative treatment	or **TMP-SMX**	2 x 5 mg TMP/kg/ day B/B/P/O 2 x 25 mg SMX/kg/day B/B/P/O	Preferred scheme if oral administration is not possible
	or **pyrimethamine** + **atovaquone** **+ folinic acid**	Day 1: 200 mg po, **then** If ≥ 60 kg; 1 x 75 mg/day P/O If < 60 kg: 1 x 50 mg/day P / O 2 x 1500 mg / day P / O (with food) 1 x 10-15 mg/day P/O	To control the myelotoxicity of pyrimethamine, mainly neutropenia
	or **sulfadiazine**	If ≥ 60 kg: 4 x 1500 mg/day P/O/B/B If < 60 kg: 4 x 1000	Sulfadiazine is associated with crystalluria and may result in renal

	+ **atovaquone**	mg/day P/O/B /B 2 x 1500 mg/day P/O (with food)	insufficiency and urolithiasis. Good hydration is important. Check your kidney function and urine sediment for microhematuria and crystalluria.
	or **pyrimethamine** + **azithromycin** + **folinic acid**	Day 1: 200 mg P/O, followed by If ≥ 60 kg; 1 x 75 mg/day P/O If < 60 kg: 1 x 50 mg/day P/O 1 x 900-1200 mg/day P / O 1 x 10-15 mg/day P/O	To control the myelotoxicity of pyrimethamine, mainly neutropenia
Secondary Prevention / Supportive Care			
Stop: if CD4 > 200 cells/μL and HIV VN undetectable for more than 6 months			
The listed schemes are used as alternatives	**sulfadiazine**	2-3 g / day P / O (in 2-4 doses)	
	+ **pyrimethamine**	1 x 25-50 mg/day P/O	
	+ **folinic acid**	1 x 10-15 mg/day P/O	
	or **clindamycin**	3 x 600 mg/day P/O	Additional prevention of PCP is important
	+ **pyrimethamine**	1 x 25-50 mg/day P/O	
	+ **folinic acid**	1 x 10-15 mg/day P/O	
	or **Atovaquone suspension**	2 x 750-1500 mg/day P/O (with meals)	
	+ **pyrimethamine**	1 x 25-50 mg/day P/O	
	+ **folinic acid**	1 x 10-15 mg/day P/O	
	or **Atovaquone suspension**	2 x 750-1500 mg/day (s food)	
	or **TMP-SMX**	1 table. Double dosage (800/160 mg) 2 h/day P/O	

Cryptococcal meningitis

Treatment
14 days of induction therapy, followed by 8 weeks of consolidation therapy, then secondary prophylaxis for at least 12 months. Stop if CD4 count > 100 cells/μL and HIV VN is undetectable for more than 3 months **Diagnosis:** positive microscopy OR antigen detection, OR culture in cerebrospinal fluid **Manifestations in other organs:** Cryptococcal infection can also cause pneumonia, which can be difficult to distinguish from Pneumocystis pneumonia. The infection can also affect other organs and be disseminated. Primary prevention: Primary prevention: the results of a large randomized clinical trial in Africa (REALITY study [9]) suggest that enhanced prevention of infection in individuals with severe

immunosuppression (<50 CD4 cells/µL), including isoniazid for 12 weeks, fluconazole 100 mg/day for 12 weeks, azithromycin 500 mg/day for 5 days, and a single dose of albendazole 400 mg may generally reduce opportunistic infections (includingcryptococcal meningitis) and mortality.

Preventive therapy: The early stages of generalized cryptococcal infection may be asymptomatic. New data from under-resourced settings support the need for cryptococcal antigen serum analysisamong all patients,

who have been diagnosed with HIV infection with CD4 < 100 cells/µl. If cryptococcal antigen is detected, cerebrospinal fluid should be examined to rule out cryptococcal meningitis. If meningitis is excluded, preventive therapy with fluconazole 800 mg / day SC is recommended for two weeks before

initiation of cART to reduce the risk of IVS.

	Preparation	**Dose**	**Comments**
Prevention therapy	**fluconazole**	1 x 800 mg/day O/O for 2 weeks, followed by 1 x 400 mg/day O/O within 8 weeks	In the case of: - Positive serum test result for cryptococcal antigen - Asymptomatic course - Cryptococcal meningitis is excluded by CSF examination
Induction therapy	**liposomal amphotericin B + flucytosine**	3 mg/kg/day B /B 4 x 25 mg/kg/day/P/O	**14 days** - Then perform a lumbar puncture (LP): if the CSF culture is sterile, switch to an oral regimen . -When performing LP, the opening pressure should always be measured. -Repeated LP or cerebrospinal fluid bypass surgery is necessary to effectively control the increased intracranial pressure associated with better survival -Corticosteroids, which are ineffective in lowering increased intracranial pressure, can be harmful and their use is contraindicated -Dosages of flucytosine should be adapted to renal function - Delay the initiation of cART for at least 4 weeks. -Amofotericin B deoxycholate may not be available in all European countries -Flucytosine may not be available in all European countries. Consider substitution with fluconazole 2 x 400 mg/day in The course of the induction phase
	or amphotericin B deoxycholate + flucytosine	0.7 mg/kg/day B /B 4 x 25 mg/kg/day P/O	
Consolidation therapy	**fluconazole**	1 x 400 mg/day (loading dose 1 x 800 mg on the first day)	8 weeks. Repeated LP until the opening pressure is <20 cm H_2O
Secondary Prevention / Supportive Care			

At least 12 months **Consider discontinuation:** if CD4 count >100 cells/μL and HIV VN is undetectable for more than 3 months			
	fluconazole	1 x 200 mg/day P/O	see Interactions of ARVs with others Medicines
Oropharyngeal candidiasis			
Diagnosis: typical clinical manifestation, see Interaction of ARVs with other drugs means, for all azole preparations			
Preferred alternate willow	**fluconazole**	1 x 150-200 mg/day P/O	Once or until improvement (5-7 days)
	Itraconazole	1-2 x 100-200 mg/day P/O (oral solution on an empty stomach)	7-14 days. Be mindful of the interaction with ART, see Interaction of ARVs with other drugs
	nystatin	3-6 lozenges of 400000 units (approx. 4-6 ml)/day	7-14 days
	or amphotericin B	3-6 lozenges in 10 mg / day or P / O suspension 1-2 g / day (in 2-4 receptions)	
Esophagitis			
Definitive diagnosis: macroscopic examination by endoscopy, OR histology of the biopsy, OR cytology of the sample from the surface of the mucous membranes **Preliminary diagnosis:** if 1.Recent onset of dysphagia AND 2. Oropharyngeal candidiasis			
Preferred alternate willow	**fluconazole**	1 x 400 mg/day or 400 mg loading dose, followed by 200 mg/day P/O	3 days 10-14 days
	consider **itraconazole** or **posaconazole or voriconazole or caspofungin**	1-2 x 100-200 mg / day P / O (solution for P / O-th intake on an empty stomach) 2 x 400 mg/day P/O 2 x 200 mg/day P/O 1 x 70 mg / day IV, after 1 x 50 mg / day IV	10-14 days. Be aware of the interaction with ART, see Interaction of ARVs with other drugs In case of refractory disease, treat according to the results of the resistance test. Choose the dosage of posaconazole and voriconazole in accordance with minimum inhibitory concentration of candida and minimum level drug in the blood.

Histoplasmosis (Histoplasma capsulatum)

Treatment

Diagnosis: Detection of antigen in blood, urine, or bronchoalveolar fluid OR positive microscopy OR mycological culture of blood, urine, broncho-alveolar fluid, cerebrospinal fluid, or tissue biology
Note: The cerebrospinal fluid that usually shows lymphatic pleocytosis is usually microscopic and shows a negative culture. Detection of hypsum antigen or antibody is more sensitive. Despite this, clinical diagnosis is possible in the case of a negative antigen or antibody of gypsoplasma in the cerebrospinal fluid, if disseminated histoplasmosis is present, and the CNS infection is not explained by another cause.

Consult an expert if you are intolerant to fluconaseol, voriconazole, or posaconazole.
Be aware of azole interactions with ART
It is recommended to measure the concentration of itraconazole and voriconazole in the blood plasma to guide optimal treatment.

	Preparation	**Dose**	**Comments**
Severe disseminated histoplasmosis	**Induction therapy: liposomal amphotericin Consolidation** **Therapy: Itraconazole**	3 mg/kg/day IV 3 x 200 mg/day O /O in for 3 days, then 2 x 200 mg/day P/O	Within 2 weeks or until improvement At least 12 months
Moderate disseminated histoplasmosis	**Itraconazole**	3 x 200 mg/day O /O in for 3 days, then 2 x 200mg/day P/O	At least 12 months
Histoplasma meningitis	**Induction therapy: liposomal amphotericin B** **Consolidation Therapy: Itraconazole**	5 mg/kg/day B /B 2 x or 3 x 200 mg/day P/O	4-6 weeks At least 12 months and until the abnormal results of the cerebrospinal fluid normalize. Measure the plasma concentration of itraconazole Blood.
Secondary Prevention / Supportive Care			
Stop: if CD4 count > 150 µL/µL, HIV ART and VN undetectable > 6 months, negative fungal blood culture, histoplasma antigen < 2 µg/L, and > 1 year of treatment **Consider long-term suppressive therapy** in **severe cases** of **meningitis and in case of recurrence despite adequate treatment**			
	Itraconazole	1 x 200 mg/day P/O	
	or **fluconazole**	1 x 400 mg/day P/O	
Treatment			
Diagnosis: antigen/PCR/smear/cerebrospinal fluid culture /biopsy. Clinical appearance skin lesions are not reliable			
Initial HSV genital/skin and mucous membranes	**valacyclovir**	2 x 1000 mg/day P/O	7-10 days or up to Curing lesions
	or **famciclovir**	2 x 500 mg/day P/O	7-10 days or up to Curing lesions

	or **acyclovir**	3 x 400-800 mg/day P/O	7-10 days or up to Curing lesions
Recurrent genital/skin and mucous HSV (> 6 episodes/year)	**valacyclovir**	2 x 500 mg/day P/O	Chronic suppressive therapy. Alternatively, begin early treatment of relapses as described above
Severe lesions of the skin and mucous membranes	**acyclovir**	3 x 5 mg/kg/day IV	After the lesions begin to regress, switch to oral therapy or until cure Lesions
Encephalitis	**acyclovir**	3 x 10 mg/kg/ day IV	14-21 days
HSV infection of the skin and mucous membranes with resistance to acyclovir	**Foscarnet**	2-3 x 80-120 mg/kg/ day IV	Prior to clinical response
Varicella-zoster virus (VZV) infections			
Treatment			
Diagnosis: typical clinical presentation with/without antibody testing OR antigen / PCR / testing / smear/cerebrospinal fluid culture /biopsy			
	Preparation	**Dose**	**Comments**
Primary chickenpox infection (chickenpox)	**valacyclovir**	3 x 1000 mg/day P/O	5-7 days
Herpes Zoster (shingles): Not disseminated	**valacyclovir**	3 x 1000 mg/day P/O	7-10 days
	or **famciclovir**	3 x 500 mg/day P/O	7-10 days
Herpes Zoster: disseminated	**acyclovir**	3 x 10 mg/kg/day IV	10-14 days
Encephalitis (including vasculitis)	**acyclovir**	3 x 10-15mg/kg/day	14-21 days
Cytomegalovirus infections (CMV			
Treatment			
Diagnosis of retinitis: clinical appearance of typical retinal lesions and response to therapy. PCR of the aqueous and vitreous body optional Diagnosis of esophagitis/colitis: endoscopic presence of ulceration and typical histological picture (porous/intranuclear corpuscle inclusions) Diagnosis of encephalitis/myelitis: clinical appearance and positive PCR result fromcerebrospinal fluid Testing of antibodies and PCR in the blood is not useful for the diagnosis of organ diseases- Targets			
	Preparation	**Dose**	**Comments**
Retinitis, directly threatening vision lesions	**ganciclovir**	2 x 5 mg/kg/day IV	21 days, then secondary prophylaxis
	or **foscarnet**	2 x 90 mg/kg/ day IV	
Retinitis, small peripheral retinal lesions	**valganciclovir**	2 x 900 mg/day (s food)	14-21 days, then Secondary prevention
	or **foscarnet**	2 x 90 mg/kg/ day IV	
	or **cidofovir + probenecid + NaCl 0.9% hydration**	1 x 5 mg/kg/day IV	2 weeks then every 2 weeks Cidofovir may not be available in all

			European countries
Esophagitis/colitis	**ganciclovir**	2 x 5 mg/kg/day IV	3-6 weeks respectively, until the disappearance of symptoms
	or **foscarnet**	2 x 90 mg/kg/ day IV	
	or **valganciclovir**	2 x 900 mg/day P/O (with food)	In milder forms of the disease, if oral treatment Transferred
Encephalitis/myelitis	**ganciclovir and / or** **Foscarnet**	2 x 5 mg/kg/day IV 2 x 90 mg/kg/ day IV	Until symptoms disappear and CMV replication in the cerebrospinal fluid ceases (with negative CSF PCR). Treatment individually according to clinical symptoms and response to treatment
Secondary Prevention / Supportive Therapy : Cytomegalovirus Retinitis			
Stop: if the CD4 count > 200 cells/μL and the HIV VN is undetectable for more than 3 months			
The listed schemes are used as alternatives	**valganciclovir**	1 x 900 mg/day (s food)	
	or **ganciclovir**	1 x 5 mg/kg/day (x 5 days/week) IV	
	or **Foscarnet**	1 x 90-120 mg/kg/day (x 5 days/week) IV	
	or **Cidofovir + probenecid + NaCl 0.9% hydration**	1 x 5 mg/kg every 2 weeks IV	Cidofovir may not be available in all European countries
Treatment			
Definitive diagnosis (laboratory): evidence of JCV-DNA in CSF AND the presence of a compatible clinical and radiological picture **Definitive diagnosis (histology):** typical histological results along with in-situ manifestation of JCV-DNA antigen or JCV-DNA And the presence of a compatible clinical-radiological picture **Preliminary diagnosis:** compatible clinical and radiological picture if JCV-DNA in CSF negative or not detected			
Patient not taking ART	Start cART immediately The use of AI may be preferable and justified, given the importance of rapid recovery of the immune system in PML. Particular attention should be paid to the development of WSVI		
Patient taking ART, failure of HIV VN suppression	Optimize cART The use of AI may be preferable and justified, given the importance of rapid recovery of the immune system in PML. Particular attention should be paid to development		
A patient who has not been taking ART formany years	Continue with the current cART		

weeks-months or at effective cART			
	Note: there is no specific treatment for JCV infection that has proven effective in PML other than rare case histories, so it is not recommended to use the following drugs that have previously or sometimes been used in PML: Alpha-IFN, sidofovir, corticosteroids (with the exception of treatment of VSVI-PML), cytarabine, intravenous immunoglobulins, mefloquine, mirtazapine and topotecan		
Treatment of immune reconstitution syndrome (VSVI)			
Diagnosis: - Paradoxical VSVI: paradoxical worsening of symptoms in the context of ART-induced immune recovery.			
Treatment: - Corticosteroids, for example, a high dose of prednisolone (for example, 90 mg / day for 3-5 days) or intravenous dexamethasone (for example, 0.3 mg / kg / day for 3-5 days), followed by a gradual decrease in the dose of P / O for 1-6 weeks. Note: Theuse of corticosteroids is not recommended in individuals without signs of inflammation. There are no other treatments that have been proven effective in treating IVVI other than rare cases of histories Disease			
Bacterial angiomatosis (Bartonella **henselae, Bartonella quintana)**			
Treatment			
Diagnosis: typical histology			
	Preparation	**Dose**	**Comment**
	Doxycycline	2 x 100 mg/day P/O	Prior to improvement (up to 2 months) Possible interaction with ARVs Drugs
	or **clarithromycin**	2 x 500 mg/day P/O	
Primary prevention			
Consider prophylaxis only if there is no clinical suspicion of the spread of non-uberulosis bacteria. **Prophylaxis may be delayed if ART has been started within four weeks.** **Stop:** If the CD4 > 100 cells/μL for more than 3 months and the patient is on effective ART (and, according to experts, VN HIV is undetectable)			
The listed schemes are used as alternatives	**azithromycin**	1 x 1200-1250 mg/ Week P/O	Check on interaction with ARVs
	or **clarithromycin**	2 x 500 mg/day P/O	
	or **Rifabutin**	1 x 300 mg/day P/O	Check on interaction with ARVs
Treatment			
Diagnosis: clinical picture and cultures of blood, lymph nodes, bone marrow or other commonly sterile samples. For any treatment regimen, check for interactions with ARVs			
***Mycobacterium avium-intracellulare* complex (MAC)**			
Preferred schemes	Preferred	Preferred	Preferred schemes

	circuitry	circuitry	
	or **azithromycin** **+ ethambutol**	1 x 500 mg/day P/O 1 x 15 mg/kg/day P/O	Consider additional medications as described above
Mycobacterium kansasii			
	Rifampicin **+ isoniazid** **+ ethambutol**	1 x 600 mg/day SC (or rifabutin 300 mg/day SC) 1 x 300 mg/day P/O 1 x 15 mg/kg/day P/O	12 months after negative culture
	or **Rifampicin** **+ clarithromycin** **+ ethambutol**	1 x 600 mg/day SC (or rifabutin 300 mg/day SC) 2 x 500 mg SC 1 x 15 mg/day P/O	12 months after negative culture
Secondary Prevention / Supportive Care			
Stop: if CD4 count > 100 cells/μL and HIV VN is undetectable for 6 months and treatment MAC takes at least 12 months			
Mycobacterium avium (MAC) infection These regimens are used as alternatives	**clarithromycin** **+ ethambutol**	2 x 500 mg/day P/O 1 x 15 mg/kg/day P/O	
	or **azithromycin** **+ ethambutol**	1 x 500 mg/day P/O 1 x 15 mg/kg/day P/O	
Cryptosporidiosis (C. parvum, C. hominis)			
Treatment			
Diagnosis of AIDS-associated cryptosporidiosis can be carried out only in cases of severe immunodeficiency (CD4 lymphocyte count <100 cells / μl) and chronic diarrhea (> 4 weeks) using immunofluorescence or Ziehl-Nielsen staining of stool or tissue. Themain focus of therapy is the use of ART to restore immune competence with CD4 > 100 cells/μL. In addition, additional measures are symptomatic treatment, rehydration and correction of deficiency and compensation for loss All antiprotozoal therapies can be used in addition to cART in severe cases, but this is not enough to achieve the destruction of protozoa without restoring immunity.			
	Preparation	**Dose**	**Comment**
	nitazoxanide	2 x 500-1000 mg/day P/O	14 days
	or **paromomycin**	4 x 500 mg/day P/O	14-21 days
Treatment			
Diagnosis of AIDS-associated cystoisosporosis can only be carried out in the case of chronic diarrhea (> 4 weeks) using UV fluorescence or microscopy of the stool, duodenal material or biopsy of intestinal tissue. In addition to antiprotozoal treatment, additional measures are symptomatic treatment, rehydration and correction of deficiency and compensation for the loss of electrolytes.			
	Preparation	**Dose**	**Comment**

Preferred therapy	**TMP-SMX**	2 x 2 tablets of double dosage (800/160 mg) / day P / O or 2 x 1 double-dosage tablets (800/160 mg) / day P/O	minimum 10 days, increase the duration of treatment to 3-4 weeks if symptoms worsen or persist 10 days, zoom in dosage up to 2 x 2 tablets of double dosage/day if Symptoms worsen or persist
Alternative therapy for intolerance to TMP-SMX	**pyrimethamine + leucovorin** or **ciprofloxacin**	1 x 50-75 mg/day P/O 1 x 10-15 mg/day P/O x 500 mg/day P/O	10 days When pyrimethamine is used, it is necessary to monitor for the development of myelotoxicity, mainly neutropenia 7 Days
Secondary Prevention / Supportive Care			
Stop: if the CD4 count > 200 cells/μL, the HIV VN is undetectable for more than 6 months and there are no signs of persistent cytoisporosis			
Preferred therapy	**TMP-SMX**	1 tablet of double dosage (800/160 mg) 3 x /week P / O or 1 table. double dosage / day P / O table. double dosages 3 x/week P/O	
Alternative therapy	**pyrimethamine + leucovorin**	1 x 25 mg/day P / O 1 x 10-15 mg / day P / O	When using pyrimethamine, it is necessary to monitor for the development of myelotoxicity, in mainly, neutropenia
Leishmaniasis			
Treatment			
Diagnosis: microscopy or PCR in smears, body fluids or tissues			
Preferred therapy	**liposomal amphotericin B**	4 mg/kg every 2-4 weeks IV	
	or **amphotericin B (lipid complex)**	3 mg/kg every 3 weeks IV	

Alternative therapy	**pentavalent salt antimony (Glucantime®)**	20 mg / kg / day IV or IM	
	or **Miltefosine**	1 x 100 mg/kg/day P / O	
	or **pentamidine**	300 mg every 3 to 4 weeks IV	

Annex 12

Dyslipidemia

Principles: With an increase in LDL cholesterol, the risk of CVD increases, and with a decrease in it, this risk decreases (see the table below, which presents the drugs used for this indication). For HDL cholesterol, there is probably an inverse relationship, but the results of thestudies are less conclusive. As for the dependence of the risk of CVD on an increase in triglyceride levels above normal, it is even less obvious, since it has never been properly shown that this level alone makes it possible to judge the risk of CVD. Moreover, the clinical efficacy of treatment of moderate hypertriglyceridemia is not obvious; at very high levels of TG (> 10 mmol/L or > 90 mg/dL), the risk of pancreatitis may increase.

Reducing calorie content, increasing the level of physical activity, weight loss and quitting smoking usually contribute to the correction of HDL levels. Consuming fish, reducing calorie intake, saturated fat, and alcohol lowers triglyceride levels. If there is no result, you should consider switching to another ART regimen, and then consider prescribing lipid-lowering drugs. Statins should be given to all patients diagnosed with vascular disease, including patients with CI abet type 2 or a high risk of CVD, regardless of lipid levels.

Drugs used to lower LDL cholesterol

Preparation class	**Preparation**	**Dose**	**Side effects**	**How to use statins with ART**	
				Reception with PI / r	**Admission with NNRTIs**
Statin (I,IX)	atorvastatin(II)	10-80 mg 1p / day	Symptoms from the gastrointestinal tract, headache pain, insomnia, rhabdomyolysis (rare) and toxic hepatitis	Start with a low dosage (V) (maximum: 40 mg)	Higher dosage (VI) possible
	fluvastatin(III)	20-80 mg 1r / day		Higher dosage (VI) possible	Higher dosage (VI) possible
	pravastatin(III)	20-80 mg 1r / day		A higher dosage (VI, VII)	Higher dosage (VI) possible
	rosuvastatin(II)	5-40 mg 1p / day		Start with a small one Dosage (V)	Start with a low dosage (V)

				(maximum: 20 mg)	
	simvastatin(II)	10-40 mg 1p / day		Contraindicated	
Inhibition of absorption of cholesterol in the intestine↓ (I,VIII)	Ezetimibe (IV)	10 mg 1p / day	Gastrointestinal symptoms	No known drug interactions with ART	
Ingibitor PCSK9 (X)	Evolocumab	140 mg 2 p / week or 420 mg 1 p / month	Zero	No drug interactions are expected	

Statins are preferred as first-line therapy; different statins have different ability to lower LDL cholesterol

II, III, IV Target LDL cholesterol levels: see page 41. Patients who find it difficult to lower LDL cholesterol to target levels should be referred to a specialist.

Expected LDL cholesterol reduction ranges: II 1.5-2.5 mmol/L (60-100 mg/dL), I II 0.8-1.5 mmol/L (35-60 mg/dL), IV 0.2-0.5 mmol/L (10-20 mg/dL)

V , VI ART drugs can v inhibit the excretion of statins (statin toxicity, dose reduction) or vi induce it (decrease in the effectiveness of statins, gradual increase in dose to achieve the expected result II, III)

VII Exception: if the patient is taking DRV/r, then a lower dose of pravastatin should be started.

VIII This drug can be prescribed to patients with HIV infection who do not tolerate statins, or used in conjunction with a statin with an insufficient decrease in LDL levels, despite the maximum tolerated statin.

IX Experimental morbidity/mortality data for pitavastatin are not yet available for adjudication recommendations for its use, but the drug may haveadvantages manifested in less drug-drug interaction, increased HDL levels and a lower level of negative effects on glucose compared to other statins.

X Their administration should be considered to patients with high risk and insufficientexposure to maximum doses of statins or with intolerance to statins.

Annex 13

Bone diseases : detection and diagnosis

Disease	**Characteristics**	**Risk** factors	**Diagnostic tests**
Osteoporosis Postmenopausal women and men aged ≥ 50 years whose BMD has a T-score ≤ -2,5	Reduced bone mass Increased incidence of fractures in HIV-infected people	To evaluate classical risk factors(II) and fracture risk using FRAX. Consider DXA research for all	DXA Scan Exclude the causes of secondary osteoporosis with abnormal BMD values low (VI)

<table>
<tr>
<td>Premenopausal women and men aged < 50 years who have BMD Z-score ≤ -2 and pathological fracture</td>
<td>It is asymptomatic until the first fracture

Common in HIV
The prevalence of osteoporosis is up to 10-15%
Multifactorial etiology
Reduction of BMD,
observed at the beginning of ART
A significant decrease in BMD at the beginning of somex ARVs (I)</td>
<td>patients who have ≥ 1 risk:(iii)
Postmenopausal women Men ≥ 50 years old
Patients aged 40-50 years with a high risk of fractures (>20% 10-year risk of fractures based on FRAX score without DXA)
History of low-traumatic fracture
High risk of falls (IV) Clinical hypogonadism (symptomatic - see
Sexual dysfunction) Taking oral glucocorticoids (at least 5 mg of prednisone or equivalent per day for >3 months)
For patients with the above-mentioned risk factors, it is advisable to perform DXA before initiating ART. To assess the impact of risk factorson fracture risk by including DXA results in the FRAX® score (www.shef.ac.uk/FRAX) Use only in patients over 40 years of age
There may be an underestimationof the risk for HIV-infected patients
HIV can be considered as indirect cause(V) of osteoporosis</td>
<td>Lateral radiograph of the spine (lumbar and thoracic) with low BMD of the spine, in case of detection of osteoporosis by DXA, as well as if there is a significant loss of growth or kyphosis develops. (Alternatively, to assess the risk of spinal fracture, instead of a lateral radiograph, you can use DXA scanning).</td>
</tr>
<tr>
<td>Osteomalacia</td>
<td>Impaired bone mineralization
Increased risk of fractures and bone pain Vitamin D deficiency can cause weakness of the proximal muscles
High prevalence (>80%)
Failure vitamin D in some HIV+</td>
<td>Dark skin Malnutrition Seeking to avoid exposure to sunlight Malabsorption
Obesity
Loss of phosphates (VII) through the kidneys</td>
<td>In all patients, measure 25-OH-vitamin D at diagnosis

<table><tr><td></td><td>ng/ml</td><td>NMOl/l</td></tr><tr><td>Defit IT</td><td>< 10</td><td>< 25</td></tr><tr><td>Nedost Exactly the</td><td>< 20</td><td>< 50</td></tr></table>
In case of deficiency or insufficiency, check the PTH level. Consider replacing vitamin D, with</td>
</tr>
</table>

	cohorts and y of the general population		availability of clinical Readings.
Osteonecrosis	Infarction of the epiphyseal cartilage of long bones, causing acute bone pain The disease is rare, but among HIV-Infected prevalence See above.	Risk factors: Low CD4 levels Glucocorticoid Use Injecting Drugs	MRI

I Significant reduction in BMD observed at the beginning of treatment regimens containing TDF or some PIs. Additional BMD losses observed during transitions to a TDF-containing ART regimen, and BMD recovery during transitions from such regimens to any other regimens. The clinical significance for the assessment of fracture risk has not been determined. TAF does not demonstrate undesirable effects on bone tissue like TDF. Consider replacing TDF* with non-tenofovir or TAF** if the patient has:

- Osteoporosis / progressive osteopenia
- History of pathological fracture
- FRAX Calculator for Major Osteoporotic Fracture > 10%
- PI as a third drug

* Expert opinion, results of clinical trials are expected

** The amount of data on the use of TAF in oGFR ≤ 30 mL/min is limited; The long-term results are unknown.

II Classic risk factors: age (older than average), female sex, hypogonadism, family history of hip fracture, low BMI (≤19 kg/m2), vitamin D deficiency, smoking, lack of exercise, history of low-traumatic fracture, excessive alcohol consumption (>3 standard doses per day), steroid use (minimum 5 mg prednisone per day or equivalent for
>3 months).

III If the T-score is normal, repeat after 3-5 years in groups 1, 2 and 5; if the risk factors do not change, then there is no need for re-screening with DXA in groups 3 and 4; Re-screening is needed only in GroupPE 6 if steroid use continues.

IV Methodology and Toolkit for Fall Risk Assessment (FRAT) https://www2. health.vic.gov.au/ageing-and-aged-care/wellbeing-and-participation/healthy-ageing/ falls-prevention/falls- prevention-tools

V If you include the BMD parameter when calculating with the FRAX calculator, the answer "yes" in the secondary cause cell will not be considered when using the FRAX algorithm, since it is assumed that secondary osteoporosis affects the risk of fractures only through the BMD. However, if HIV infection contributes to an increased risk of fractures in part independent of BMD, the probability of fractures may be underestimated by the FRAX calculator.

VI The causes of secondary osteoporosis include: hyperparathyroidism, hyperthyroidism, lowabsorption, hypogonadism/amenorrhea, diabetes mellitus, chronic liver disease.

VII On the diagnosis and treatment of phosphate loss through the kidneys.

Annex 14

Diagnosis of kidney disease

oGFR(i)				
> 60 ml/min		**> 60 ml / min, but there is an accelerated decrease oGFR***	**> 30 - ≤ 60 ml/ min**	**≤ 30 ml/min**
PROTEINURII (ii)	BM/C(iii) < 50	Regular observation		· Monitor risk factors for CKD and the use of nephrotoxic drugs, including ART(iv). · If necessary, cancel or change the dosage of medicines (v) · Perform ultrasound of the kidneys · In urgent cases, consult a nephrologist
	BM/K(iii) 50-100	· To assess the risk factors for CKD(viii) and nephrotoxicity of drugs, including ARVs (iv, viii) · If necessary, cancel or change the dosage of medicines (v) · Conduct an ultrasound of the kidneys · With hematuria and any level of proteinuria, refer to a nephrologist · In the case of a new XRP or an increasing decrease in oGFR, refer to Nephrologist		

* Defined as a 5 mL/min reduction in oGFR per year for ≥3 consecutive years, or a 25% decrease in oGFR from baseline has been confirmed.

Treatment of HIV-associated kidney disease (VI)

Prevention of progressive renal disease Failure	**Notes**
1. ART	Initiate ART immediately for HIV-associated nephropathy (VICHAN)(VII) or serious suspected immune complex disease in HIV. Immunosuppressive therapy may contribute to the manifestation of immunocomplex hypersensitivity. Kidney biopsy is recommended for histological confirmation. Consider replacing TDF** with non-tenofovir or TAF*** if: - BM/K 20-50 mg/mmol oGFR > 60 ml/min, but there is a decrease in oGFR by 5 ml/min per year for at least 3consecutive years or a 25% decrease in oGFR from baseline has been confirmed comorbidities with a high risk of CKD (e.g., diabetes and hypertension), body weight < 60 kg, use of PI/r as a third drug. Consider replacing TDF** with non-tenofovir or TAF*** if: - oGFR ≤ 60 ml/min BM/K > 50 mg/mmol concomitant nephrotoxic drug had previous toxicity of TDF (proximal renal tubulopathy) ** Expert opinion pending clinical data

	There are limited data on the use of TAF in eGFR ≤ 30 mL/min, long-term effects unknown.
2. Start taking ACE inhibitors or angiotensin-II receptor antagonists if there is: - Hypertension, and/or - Proteinuria	Carefully monitor the level of oGFR and K + at the beginning of therapy and with increasing dose. a. Target blood pressure: < 130/80 mmHg Art.
3. General measures: - Avoidance of the use of nephrotoxic drugs; - Lifestyle changes (smoking, weight, nutrition); - Treatment of dyslipidemia and diabetes - If necessary, change the dosage medicines(v)	CKD and proteinuria are independent risk factors for CVD.

I For oGFR: use the SCD-EPI formula based on the following parameters: serum creatinine, gender, age and ethnicity, because quantitative analysis of oGFR is valid at >60 ml / min. Alternatively, you can use theabbreviated diet modification formula for kidney disease (sTIRD) or the Cockcroft-Gault formula.
Determination of CKD: eGFR < 60 ml/min for > 3 months (see http://www.kdigo. org/clinical_practice_guidelines/pdf/CKD/ KDIGO_2012_CKD_GL.pdf). In the absence of a history of CKD, confirm the pathological level of eGFR within 2 weeks. The use of DTG, COBI and PI boosted by RTV is associated with an increase in serum creatinine/a decrease in oGFR due to inhibition of creatinine transport
in the proximal tubules without compromising the actual glomerular filtration: set the new value after 1-2 months.
II Urinalysis: Use a strip urine test to screen for hematuria. For screening for proteinuria, use a strip urine test, and if the result ≥ 1+, then you need to check the ratio of urine protein to creatinine (BM / K) or screen BM / K. Abouttheinuria

It is considered persistent if it is confirmed in more than 2 cases with an interval > 2-3 weeks. If there is no BM/C, use the ratio of urine albumin to creatinine (AM/C), see (III).

III BM / C in a single portion of urine is preferable to AM / K, since it determines the total urine protein in glomerulopathies and tubulopathies. AM/K largely determines glomerular diseases and can (if there is no BM / C) be used for screening for HIV-associated kidney disease, but is not suitable for TFRinking for tubular proteinuria against the background of nephrotoxicity caused by drugs (for example, tenofovir).

If there are values of both indicators (BM / K and AM / K), then the ratio of BM / K > AM / K means tubular proteinuria. AM/C values for scrinning: < 30 , 30-70 and > 70. In patients with diabetes, it is necessary to monitor AM / K. BM / K is calculated as the ratio of urine protein (mg / l) to urine creatinine (mmol / l); can also be expressed in mg / mg. The coefficient for converting creatinine from mg to mmol is 0.000884.

IV Repeat urinalysis and eGFR according to the screening table

V Cm. Modification of dosages of ARVs for renal dysfunction VI Joint management of the patient together with a nephrologist.

VII VICHAN is suspected if the black race and BM/K > 100 mg/mmol and there is no hematuria.

VIII Various models have been developed to calculate the 5-year risk score for CKD using various nephrotoxic ARVs that combine HIV-independent and HIV-related risk factors

Indications and tests for proximal renal tubulopathy (PPT)

Indications for examination for proximal renal tubulopathy:	**Examination for proximal renal tubulopathy** (IV), **including:**	**Consider replacement of TDF with drugs that do not contain tenofovir, or TAF* if:**
• Progressive decrease in oGFR(i) and oGFR < 90 ml/min in the absence of other reasons and/or • Confirmed hypophosphatemia(ii) and/or • confirmed increase in BM / K (iii), • Renal insufficiency in general stable condition (GFR < 60 ml / min), • Tubular proteinuria(v).	• Blood phosphate test and excretion of phosphate in the urine (vi), • Blood glucose and glucosuria test, • Analysis of serum bicarbonate and urine pH(vii), • Determination of the level of uric acid in the blood and excretion of uric acid in the urine (viii). • Determination of serum potassium levels and excretion of potassium in the urine.	• Proximal renal tubulopathy has been confirmed in the absence of other possible causes.

I For oGFR: use the SCD-EPI formula. Alternatively , the abbreviated MDPD formula (Diet Modification for Kidney Disease) or the Cockcroft-Gault formula can be used. http://www.chip.dk/Tools

II It is determined if the serum phosphate < 0.8 mmol / l or depending on the officially accepted threshold values; exclude nephrogenic pathology of the bones, especially if the level of alkaline phosphatase is increased compared to the baseline: do tests for 25 (OH) vitamin D and PTH.

III BM / C in a single portion of urine shows total urine protein , including protein of glomerular or tubular origin.

Strip urinalysis mainly shows albuminuria as a marker of renal glomerular disease, and is not suitable for detecting tubular disease

IV It remains unclear which tests best allowyou to determine nephrotoxic

Tenofovir effect. Manifestations of proximal renal tubulopathy: proteinuria, hypophosphatemia, hypokalemia, hypouricemia, renal acidosis, glucosuria at normal blood glucose levels. Possibleconcomitant manifestations: renal failure and polyuria. Most often, only some of these disorders are observed.

V Tests for tubular proteinuria include tests for retinol-binding protein, α1 or β2 - microglobulinuria, cystatin in urine, aminoaciduria

VI It is calculated as fractional excretion of phosphate (FEphosph): (Uric acid4 (urine) / Uric acid4 (serum) / (Creatinine (urine) / Creatinine (serum)) in a single portion of urine collected inthe morning on an empty stomach. Pathology occurs at > 0.2 (> 0.1 with serum phosphate < 0.8 mmol / l)

VII Serum bicarbonate <21 mmol/L and urine pH >5.5 indicate possible renal tubular acidosis

VIII Fractional excretion of uric acid (PEmoch.k-ty): (Uric acid (urine) / Uric acid (serum) / (Creatinine (urine) / Creatinine (serum)) in a single portion of urine collected in the morning on an empty stomach. Pathology occurs at > 0.1

* In particular, if the GFR > 30 mL/min, as there are limited data on the use of TAF with GFR ≤ 30 mL/min

Application 15

Hyperlactatemia and lactic acidosis: diagnosis, prevention and treatment

Risk factors	**Prevention / Diagnosis**	**Symptoms**
· ZDV Reception · HCV/HBB co-infection · Taking ribarivine · Liver diseases · Low CD4 count · Pregnancy · Female gender · Obesity	· Standard serum lactate tracking is not recommended because it does not identify the risk of lactic acidosis. · Measurement of serum lactate, bicarbonate and arterial gases + pH is indicated in the case of symptoms suggestive of hyperlactatemia · Close monitoring of symptoms if more than 1 risk factor is present	· Hyperlactatemia: unexplained nausea, abdominal pain, hepatomegaly, increased ALT and/or AST, weight loss. · Acidemia: asthenia, dyspnea, arrhythmias. · A syndrome similar to

Treatment

Whey lactate **(mmol/L)**	**Symptoms**	**Actions**
> 5(I)	Yes/No	• Repeat the test under standard conditions to confirm and obtain arterial pH and bicarbonate(i) values If confirmed, exclude other reasons: • arterial pH ↓ and/or bicarbonate ↓(i): cancel all NRTIs; • arterial pH ↓ and/or normal bicarbonate: change of NRTI regimen from high-risk to low-risk drugs and close monitoring OR the abolition of all NRTIs
2-5	Yes	Rule out other causes; if nothing is found: carefully observe the patient OR ponder change from a high-risk NRTI to a low-risk NRTI OR cancel an NRTI

2-5	No	Repeat the test If confirmed: observe closely
< 2		No
Management of patients with lactic acidosis (regardless of serum lactate levels)		Hospitalize the patient. Cancel all NRTIs. Inject fluids intravenously. You can use vitamins (vitamin B complex forte 4 ml twice a day, riboflavin 20 mg twice a day, thiamine 100 mg twice a day; L-carnitine 1000 mg twice a day), although the benefits have not been proven.
i Lactic acidosis is a rare, life-threatening condition, usually accompanied by symptoms; high risk if serum lactate > 5 and especially > 10 mmol/L.		

Annex 16

Sexual and reproductive health of women and men living with HIV

Screening questions about sexual and reproductive health, as well as sexual function, should be asked every time an HIV-infected patient comes to see a doctor.

Sexual transmission **of HIV**

Effective measures to prevent sexual transmission of HIV include:	
Measure	**Notes**
Use of a female or male condom	· Effective for HIV-infected patients, receiving or not receiving treatment.
Post-exposure prophylaxis (PEP)	· It is recommended in all cases of unprotected or vaginal sex, when one partner is determined to have HIV and the other partner is seronegative. · You need to start as early as possible, no later than 48/72 hours after sexual intercourse.
Pre-contact Prevention (PrEP)	· Effective for HIV-negative patients with extremely risky sexual behavior
ART for an HIV-infected partner	· It is considered effective after 6 months of completely suppressive therapy, in the absence of active STIs. · It is recommended, for example, for HIV-discordant couples(i)

Screening and treatment of STIs

For all sexually active HIV-infected patients, STI screening should be performed at HIV diagnosis and annually thereafter, or in case of STI signs and pregnancy. Diagnosis should be carried out in accordance with local or national guidelines.

More detailed recommendations can be found on the http://www.iusti.org/regions/Eu rope/euroguidelines.htm

Reproductive health

Reproductive health issues should be discussed as a matter of priority with both partners, especially in discordant couples. See. Interaction of ARVs with contraceptives/hormone replacement therapy drugs.
Tips for HIV-discordant couples who want to have children.
Screening of both partners for STIs (and treatment if required) is mandatory. HIV-infected women who wish to become pregnant should:
(1) avoid prescribing triple NRTIs; from among the PI/r to prefer ATV/r; if treatment with NVP, EFV, DTG, RAL or DRV/r has already begun, it can be continued;
(2) Provide treatment for an HIV-infected partner to reduce the risk of HIV transmission to a partner who does not have it.
There is no single way to fully guarantee the prevention of HIV transmission; The following is a list of selected measures, as the degree of safety provided for HIV-discordant couples increases, provided that there are no STIs:

- Unprotectedsex during periods of maximum fertility (determined by monitoring the menstrual cycle), if the HIV-infected partner is not diagnosed with HIV;
- If the male partner is not HIV-positive: injecting seminal fluid with a syringe into the vagina during periods of maximum fertility;
- Sperm purification (to remove the virus) with or without intracytoplasmic sperm is no longer necessary, as effective ART eliminates the risk of HIV transmission at conception in HIV-infected men with undetectable HIV VN.

Disorders of sexual function
There are recommendations for the treatment of sexual dysfunction that are applicable to all groups of the population, but there are no such recommendations for women.
Contact a specialist as needed.

	Therapy	**Notes**
Chlamydia	Consider the possibility of prescribing doxycycline (100 mg 2 times a day P / O for 7-10 days, contraindicated in pregnancy) or azithromycin (1 g once P / O) with urethritis or cervicitis. For Lymphogranuloma venereum, prescribe doxycycline (100 mg 2 times a day for less than 21 days) or azithromycin (1 g once a week for 3 weeks) Alternative: erythromycin (500 mg every 6 hours P/O) or levofloxacin (500 mg per day) in within 7 days (or 21 days in the case of Lymphogranuloma venereum)	In HIV-infected people, MSM can cause treatment-resistant proctitis Consider co-infection with Neisseria gonorrhoeae
Gonorrhea	Ceftriaxone (500 mg IM once) together with azithromycin (2 g P / o once)	May cause proctitis, prostatitis and epididymitis In women, the disease is often asymptomatic High resistance to fluoroquinolones in all regions
Viral Hepatitis B Viral Hepatitis C	According to clinical protocols	Interruption of TDF, 3TC, or FTC reception may result in HBB reactivation

Human papillomavirus	There are several treatments for genital papillomas. There is no evidence that that one approach is better than the other. Consider surgical removal using laser surgery, infrared coagulation, cryotherapy, etc. Treatment of preinvasive cervical lesions, as well as intraanal and perianal lesions, should be carried out in accordance with local or national guidelines.	In most cases, the infection is asymptomatic; Recurrences of genital papillomas are common · For all HIV-infected women, a cytological examination of cervical scraping (PAP smear) is recommended. Screening for papillomas and cytology is recommended for all HIV-infected patients who engage in sex In case of detection suspiciousx cell formations are recommended to conduct anoscopy of high resolution (rectal palpation and external examination are not enough).
Genital viral herpes 2nd Sort of	Primary infection: acyclovir (400-800 mg P / O 3 times a day) or valacyclovir (500 mg P / O 2 times a day) for 5 days. see page 92	· Treatment of genital herpes virus type 2 does not prevent the transmission of HIV infection and only moderately prevents progression of HIV.
Syphilis	The "gold standard" for the treatment of patients with and without pregnancy is penicillin. Primary/secondary syphilis: benzathine penicillin G (2.4 million IU IM, once). In early syphilis, additional treatment with prednisone (20-60 mg per day for 3 days)reverts optic neuritis, uveitis, and the Jarisch-Herxheimer reaction. Latent syphilis at an advanced stage, or syphilis of unknown prolongation. Benzathine penicillin (2.4 million IU IM on days 1, 8 and 15); other options, such as doxycycline (100 mg of P / O 2 times a day) are considered less effective Neurosyphilis: Penicillin G (6x3-4 million IU IV for at least 2 weeks)	Atypical results ofthe serological test and clinical manifestations are possible. Consider cerebrospinal fluid (CSF) analysis in patients with neurological symptoms (evidence of intrathecal antibodies, pleocytosis, etc.). Successful treatment eliminatesclinical symptoms and reduces the result of the VDRL test (serological test for syphilis) by 4 times for 6-12 months

Annex 17

Depression: detection, diagnosis and treatment

- The prevalence of depression among HIV-infected people (20-40%, according to available data) is much higher than among the general population (7%).
- Depression significantly reduces the patient's capacity and weakens the effectiveness of HIV treatment.

Who to examine?	How to examine?	How to make a diagnosis?
Examination of all patients with HIV infection is recommended due to the high prevalence of depression Family history of particularly high-risk signs of depression; a depressive episode in one's own anamnesis; old age; adolescence ; history of drug dependence, psychiatric, neurological or severe somatic diseases; use of EFV the use of neurotropic drugs and recreational drugs As part of the Neurocognitive Impairment Study	Screening every 1-2 years Two main questions: Have you often experienced feelings of depression, sadness, and hopelessness in recent months? Have you lost interest in activities you used to enjoy? Special symptoms in men: – stress, burnout syndrome, outbursts of anger, immersion in work or alcohol. Exclude organic cause (hypothyroidism, hypogonadism, Addison's disease, non-ARV drugs, deficiency vitamin B12)	Symptoms (evaluate regularly): At least 2 weeks of depressed mood OR Loss of interest OR Decreased sense of pleasure And 4 out of 7 following factors: a change in body weight of ≥ 5% per month or a prolonged change in appetite; insomnia or frequent drowsiness; changes in the speed of thinking and movement; fatigue; feelings of guilt and worthlessness; decreased concentration and decision-making ability; suicidal ideation or suicide attempt(i)
i EFV is associated with a higher risk of suicidal tendencies		

Depression: treatment

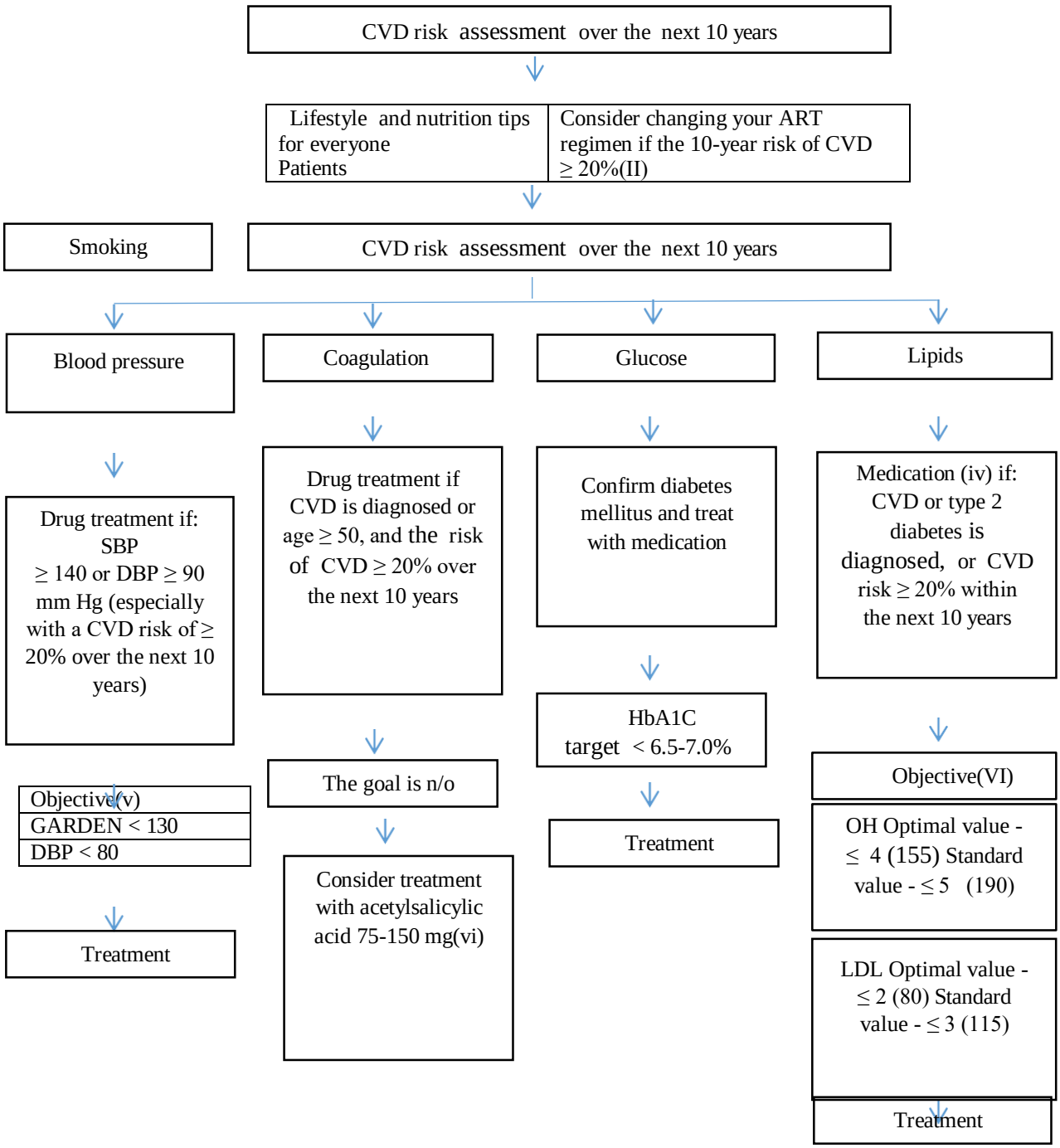
Degree of depression	Number of	Treatment	Consultation with a specialist
No	< 4	No	
Easy	4	• Problem-oriented consultation. • Consider treatment with antidepressants(i) • Recommend exercise	• Whenever the attending physician is not familiar with the use of antidepressants • If depression does not respond to treatment • If the patient has suicidal thoughts • In difficult cases (drug addiction, anxiety disorders, personality disorders, dementia, a difficult life event in acute phase)
Average	5-6	Start treatment antidepressants and(i)	
Grind	> 6	Contacting a specialist	

		(key point).	
If a patient is diagnosed with depression, it is recommended to switch from EFV to another third ARV drug in accordance with the rules for switching to a new regimen.			

Annex 18

Prevention of CVD

Principles: The intensity of CVD prevention measures depends on the baseline CVD risk that can be assessed(i). Preventive measures are diverse in nature and require the involvement of appropriate specialists, especially in high-risk CVD patients and for patients with CVD in the anamnesis - necessarily



I. Use the Framingham Scale scoring formula or any other system recommended by government regulations; there is a formula specifically designed to assess the risks of CVD in HIV-infected patients: see http://www.chip.dk/Tools. This assessment and the corresponding examinations presented in this chart should be carried out annually for all patients under observation (see pages 6-7) in order to ensure timely intervention options.

II. Options for changing the ART regimen include the following:

Replace PI/R with NNRTIs, RALs, or other PIs/R that cause fewer metabolic disorders and/or have a lower risk of CVD;

Consider replacing ZDV or ABC with TDF or using an NRTI-sparing circuit

III. For all of the above modifiable risk factors, drug treatment is indicated only for certain subgroups of patients for whom the benefits of treatment outweigh the possible harm. Attention should be paid to the fact that in the selected target groups there is a cumulative effect of various activities. Decrease in systolic pressure torovi for every 10 mm Hg. Art . Art., reduction of total cholesterol for every 1 mmol / l (39 mg / dl), the use of acetylsalicylic acid

- each of these factors reduces the risk of coronary artery disease by 20-25%; The effect is cumulative. Observational studies show that quitting smoking reduces the risk of coronary artery disease by about 50%, and this reduction adds up to reductions that are caused by other interventions.

IV Cm. discussion of drug treatment of patients with a lowerrisk of CVD at www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt. htm

V For patients at higher risk (e.g., diabetes), where possible, SBP < 130 and DBP < 80 mmHg are targeted.

VI Target levels are offered as a guideline and are not decisive. They are expressed in mmol/L, and the mg/dL value is given in parentheses. In the case where LDL cannot be calculated due to high triglyceride levels, a target level of non-HDL cholesterol (OH minus HDL cholesterol) should be used, which is 0.8 mmol/L (30 mg/dL) higher than the corresponding target LDL cholesterol level. Target values for triglycerides are not specified, since it is not known what the independent effect of their level is on CVD risk, and therefore to decide whether this disease should be treated;

VII The data indicating the effectiveness of treatment of patients without CVD in the anamnesis (including diabetics) are less convincing. In such cases, blood pressure should be properly checked before prescribing aspirin.