



Pre-exposure HIV prophylaxis in Russia: market analysis for 2022

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List of abbreviations

ARV, ART, ARVD	antiretroviral drugs
JSC	Joint-Stock Company
EECA	Eastern Europe and Central Asia region
HIV	human immunodeficiency virus
WHO	World Health Organization
SRM	State Register of Medicines
PrEP	pre-exposure prophylaxis
EACS	European AIDS Clinical Society
FDA	Federal Food and Drug Administration of the USA
UIS	Unified information system for procurement
VED	List of Vital and Essential Drugs
CJSC	Closed Joint-Stock Company
IDs	infectious diseases
STIs, STDs	sexually transmitted infections, sexually-transmitted diseases
CSW	commercial sex workers
PLH	people living with HIV
PWUD (IDU)	persons who use drugs
MoH RF	the Ministry of Healthcare of the Russian Federation
INN	International Non-proprietary Name
MHSWM	men having sex with men
RDC	research and development center
NRTI	nucleoside reverse transcriptase inhibitors
OJSC	Open Joint-Stock Company
LLC	Limited Liability Company
Rospotrebnadzor	Federal Service for Supervision of Consumer Protection and Welfare
Roszdraznadzor	Federal Service for Surveillance in Healthcare
RF	the Russian Federation
TGP	transgender persons
AIDS	acquired human immunodeficiency syndrome
USA	the United States of America
TN	tradename
FBIS	Federal Budgetary Institution of Science
FZ	federal law
FDC	fixed dose combination
AIDS Center	Center for Prevention and Control of AIDS and IDs

Introduction

The incidence and prevalence of HIV infection, as well as HIV mortality in Russia are among the highest among the countries of EECA (Eastern Europe and Central Asia). In Russia and in many other countries, including in the EECA region, there is an outflow of HIV into the general population (heterosexual contacts, partners of representatives of the key risk groups)¹. The number of new HIV infections in Russia has been consistently high over the past few years. To successfully counteract the spread of HIV, modern integrated approaches to preventive and anti-epidemic measures for HIV infection are needed. One of the extremely effective ways to prevent HIV transmission is through pre-exposure prophylaxis.

The main objective of the study is to assess the existing market of pre-exposure prophylaxis of HIV (PrEP) in Russia.

The objectives of the study are to analyze access to PrEP, analyze the demand for PrEP at all levels (state, commercial, non-commercial), establish the availability of PrEP programs and their financing, review legislation and regulations in the field of pre-exposure prophylaxis.

Based on the results of the study, conclusions were drawn about the current situation with access to PrEP in the Russian Federation and recommendations were developed to improve the accessibility of PrEP.

The situation with HIV infection in the Russian Federation

According to the Report² "HIV Infection in the Russian Federation as of December 31, 2021", since the discovery in 1987 of the first Russian infected with HIV, until December 31, 2021, the total number of detected cases of HIV infection among citizens of the Russian Federation (confirmed in the immune blot) reached 1,562,570 according to the preliminary data. As of December 31, 2021, in the country there were 1,137,596 Russians with a laboratory-confirmed diagnosis of HIV infection, excluding 424,974 patients who died during the entire observation period (27.2%).

In 2021, 71,019 new cases of HIV infection in the immune blot were reported in the Russian Federation, excluding those identified anonymously and foreign citizens, which is 1.4% less than in the same period of 2020. Last year, the death of 34,093 HIV-infected Russians was reported, which is 5.9% more than in 2020 (32,208). The number of Russians with HIV continues to increase: HIV infection is an incurable disease, and the number of new cases of HIV infection exceeds the number of deaths. As of December 31, 2021, the prevalence of HIV infection was 782.0 per 100 thousand of the population of Russia (in 2020 - 754.8), that is, 0.8% of the total population of Russia and 1.5% of the population aged from 15 to 49 years old.

¹ Financial Research Institute <https://www.nifi.ru/ru/news-ru/novosti/1552-news-010232021>

² Specialized Research Department for the Prevention and Control of AIDS of the Central Research Institute of Epidemiology of Rospotrebnadzor. The data were obtained from the territorial centers for the prevention and control of AIDS (or other authorized institutions) and the territorial departments of the Federal Service for Supervision of Consumer Protection and Welfare.

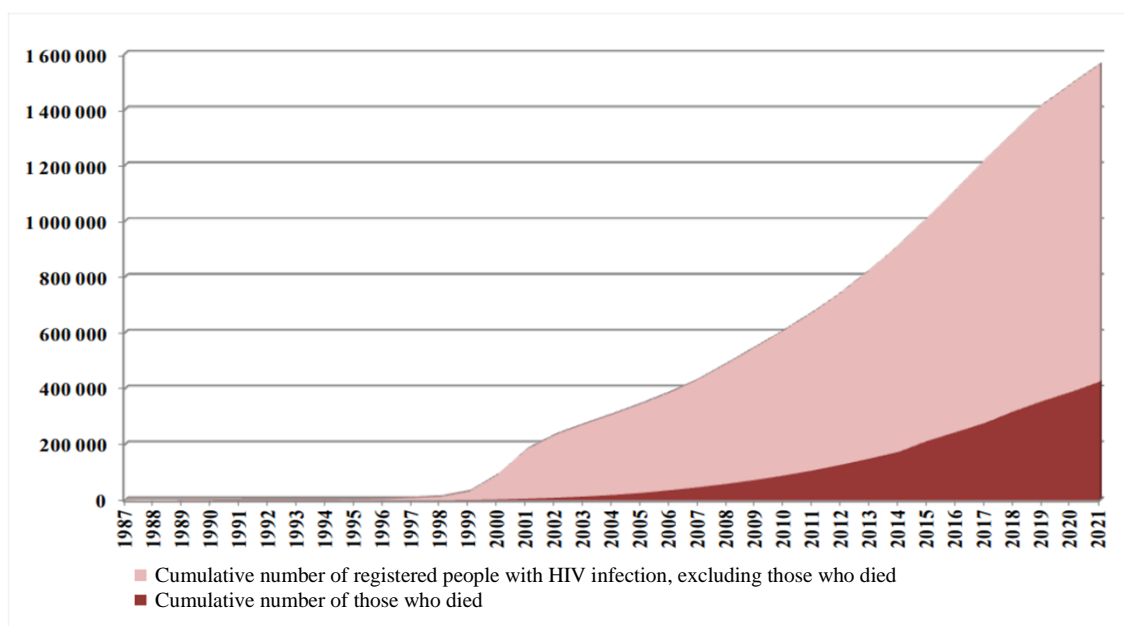


Figure 1. Cumulative number of registered people with HIV infection in Russia from 1987 to 2020

Among all Russians living with HIV, men accounted for 62.4%, however among those identified in 2021, their number decreased (59.4%) which indicates an increase in the heterosexual transmission route.

67.8% of incident patients in 2021 reported only heterosexual contacts, 27.8% reported intravenous drug use, 3.0% - homosexual contacts. Although among all identified over the period 1987-2021 HIV-positive people, more than half of them (56.9%) were infected through drug use, HIV goes beyond this group and spreads through heterosexual contact. According to the statistics, cases of virus transmission among MHSWM have become more frequent.

Despite the considerable volumes of HIV testing in Russia, the proportion of vulnerable groups (IDU, MHSWM, CSW, prisoners and STI patients) among those surveyed remains very low and continues to decline: in 2021 they amounted to 3.1% (in 2015 - 5.0%).

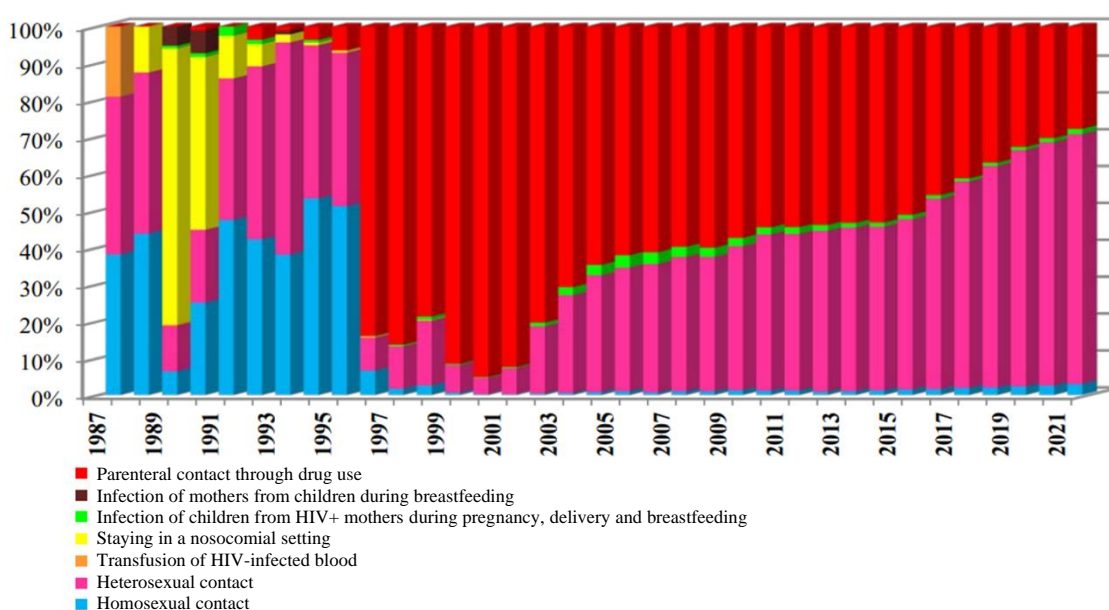


Figure 2. Distribution by ways of HIV infection in the Russian Federation in 2021 (chart from the Report of the Federal AIDS Center).

Analytical report on the method of pre-exposure prophylaxis of HIV infection using drugs

Pre-exposure prophylaxis (*PrEP*) of HIV is a method that consists in taking prophylactic antiretroviral drugs (ARVDs) to reduce the risk of possible HIV infection.

PrEP should ideally be prescribed by a doctor and taken under his/her supervision. An HIV test should be conducted before starting PrEP. Testing for sexually transmitted infections, kidney function, hepatitis B and C is also required. For PrEP to be effective, it is important that the pills are taken regularly as prescribed by the doctor. While receiving PrEP, regular visits to a healthcare facility are recommended to check for side effects and re-test for HIV, as well as for consultation.

Multiple clinical studies have shown that daily use of PrEP by HIV-negative people reduces the risk of HIV infection, is safe for patients, and is effective in preventing the spread of HIV. Up-to-date information on all ongoing, scheduled and completed clinical trials can be found in the Global PrEP Use Tracker coordinated by AVAC ([Global Advocacy for HIV Prevention](#)). The resource also allows to track the number of current PrEP projects in different countries, country registration status of drugs for PrEP, national recommendations by countries, and the cumulative number of PrEP prescriptions worldwide online. For 2022, this number was more than 3.3 million. Russia is not represented in this system.

International recommendations for the use of PrEP

In 2012, the WHO issued the first recommendations for PrEP³. The European Union approved tenofovir/emtricitabine (Truvada) for pre-exposure prophylaxis after four years. In 2015, expanded recommendations for the use of PrEP were issued⁴.

Recognizing the potential importance of PrEP, the World Health Organization (WHO) points to the importance of strict adherence to a regular drug regimen and combination of PrEP with consistent condom use and frequent HIV testing. PrEP is approved for use during pregnancy and breastfeeding.

In the USA, the use of PrEP was approved in 2012, and clinical guidelines were published in 2014.

In December 2015, South Africa became the first African country where PrEP was approved by government regulators and included in the national HIV response program. The European Medicines Agency has also granted marketing clearance for PrEP drugs in all countries of the European Union⁵.

In January 2016, France began offering PrEP under its national health care system.

In 2018, the WHO⁶ guidelines formally recognized the equivalence of tenofovir (TDF)/emtricitabine (FTC) and tenofovir (TDF)/lamivudine (3TC) regimens for PrEP. Based on the experience with antiretroviral therapy in HIV-positive people, it can be assumed that tenofovir and lamivudine taken separately are also effective.

³ Guidelines for oral pre-exposure prophylaxis (PrEP) for serodiscordant couples, men and transgender women having sex with men at high risk of HIV infection ⁴ Guidelines for initiating antiretroviral therapy and HIV pre-exposure prophylaxis

⁴ Guidelines for initiating antiretroviral therapy and HIV pre-exposure prophylaxis

⁶ Appropriate medicines: options for pre-exposure prophylaxis <https://www.who.int/publications/i/item/WHO-CDS-HIV-18.22>

⁶ Appropriate medicines: options for pre-exposure prophylaxis <https://www.who.int/publications/i/item/WHO-CDS-HIV-18.22>

In December 2021, the US FDA approved cabotegravir for injectable PrEP. The updated guidelines add a recommendation to inform all sexually active adults and adolescents about PrEP. It is important to note that the use of any other drugs and combinations instead of or in addition to those recommended is not recommended in the USA. In addition, it is forbidden to prescribe PrEP remotely (to the partner of the person who consulted the doctor) and on demand (for a single use before a risky contact).

In July 2022, the WHO released a guideline unit⁷ that lists the groups for which oral PrEP is recommended with clarification of the different regimens for each group, including for cisgender women and people who inject drugs. Also, a unit with recommendations on HIV self-testing as a tool to expand access to PrEP is included.

The 2022 EACS guidelines⁸ point out that PrEP should be used in adults at high risk of HIV infection if a condom is not used with every intercourse. With various indications, PrEP is approved in many developed and developing countries, and their list is growing every year. PrEP programs are applied in 97 countries, including in the Eastern Europe and Central Asia region (Kyrgyzstan, Ukraine).

In 2022, the WHO presented recommendations for pre-exposure prophylaxis with long-acting injectable cabotegravir.

Table 1. Groups of people for whom PrEP is recommended in international recommendations.

	WHO	EACS ⁹	USA ¹⁰
MHSWM	+/-	+	+
TGP	+/-	+	-
CSW	+/-	-	+
PWUD	+/-	-	+
Uninfected partners of patients with HIV infection (who have not achieved viral suppression)	+/-	-	+
Sexually active heterosexual persons at high risk of infection (large number of partners, irregular condom use), including:	-	+	+
with a recent STD infection	-	+	+
with recent contact for HIV post-exposure prophylaxis	-	+	+
having sex while under the influence of drugs	-	+	+/-
Prisoners	+/-	-	-

Since 2016, the WHO has abandoned the formal identification of target populations that can be offered pre-exposure prophylaxis in favor of a single criterion: the probability of infection > 3%. However, the WHO continues to distinguish populations in which the risk of infection is commonly the highest. In the table, they are marked with a "+/-" sign, since depending on the specific situation they may or may not be included in the target groups¹¹.

⁷ Differentiated and simplified pre-exposure prophylaxis for HIV prevention: update of the WHO implementation guidance <https://www.who.int/publications/i/item/9789240053694>

⁸ https://www.eacsociety.org/media/guidelines-11.0_ru_fin_interactive.pdf

⁹ https://www.eacsociety.org/media/guidelines-11.0_ru_fin_interactive.pdf

¹⁰ Centers for Disease Control and Prevention: US Public Health Service: PrEP for HIV Prevention in the United States - 2021 Update: Clinical Practice Guidelines. <https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf>

¹¹ Research report "Conducting a Socio-Economic Study on the State Policy of Combating HIV" <https://www.nifi.ru/ru/news-ru/novosti/1552-news-010232021>

Options for drug pre-exposure prophylaxis

There are two combinations of HIV drugs that are labeled for use as PrEP:

Pills: emtricitabine/tenofovir disoproxil fumarate.

It is generally recommended to daily take emtricitabine/tenofovir disoproxil fumarate (TN Truvada) as PrEP. This maintains the necessary concentration of drugs in the body. When taken daily, PrEP is effective for men and women, cisgender and transgender people, heterosexuals, and men who have sex with men.

Pills: emtricitabine/tenofovir alafenamide.

The US FDA approved the use of emtricitabine/tenofovir alafenamide (TN Descovy) in adult men and adolescents as daily PrEP in 2019. In Europe, the patent holder did not register this indication¹², in Russia, registration of this combination for PrEP is also not planned¹³.

Relatively recently, an innovative method of injection pre-exposure prophylaxis with cabotegravir has appeared.

Currently, injectable forms of PrEP and dual therapy in the form of a combination of oral contraceptives and PrEP preparations are being studied around the world.

The following active ingredients are currently approved for oral PrEP:

- tenofovir or tenofovir alafenamide;
- emtricitabine or lamivudine.

Possible oral combinations:

- tenofovir/emtricitabine;
- tenofovir/lamivudine;
- tenofovir alafenamide/emtricitabine;
- tenofovir alafenamide/lamivudine.

There are two regimens of taking oral PrEP:

- 1) PrEP regular regimen (take the drug in one dose once a day, daily). This regimen is preferable, as it significantly increases the efficiency of the method.
- 2) Situational oral pre-exposure prophylaxis (a double dose of drugs is taken at least 2 hours and no more than 24 hours before a risky contact and then one dose after 24 and 48 hours, respectively).

Legislative situation in Russia

An analysis of the legislative and regulatory framework revealed a number of contradictions in the regulations regarding the use of pre-exposure prophylaxis in Russia.

¹² <https://itpc-eeca.org/2021/10/22/gilead-ne-budut-registrirovat-novuyu-opcziyu-dokumentnoj-profilaktiki-vich-v-es/>

¹³ <https://www.eeca-cat.info/wp-content/uploads/2021/03/Protokol-Gilead-09.03.2021-final.pdf>, p.6

The provision of assistance to HIV-positive citizens in the Russian Federation is regulated by the Federal Law dated March 30, 1995, No. 38-FZ “On Preventing the Spread of Disease Caused by the Human Immunodeficiency Virus (HIV) in the Russian Federation” (as amended on July 14, 2022)¹⁴. The law specifies articles that can be applied to modern methods of HIV prevention, including PrEP, for example:

Article 4. Guarantees of the state

1. The state guarantees:

Regular informing of the population, including through the mass media, about **available measures to prevent HIV infection**;

Article 15. Prevention, diagnosis, and treatment of HIV infection

The relevant federal executive authorities coordinating scientific research ensure the development and **implementation of modern methods for the prevention**, diagnosis, and treatment of HIV infection, and also submit for approval by the Government of the Russian Federation a draft federal targeted program aimed at **preventing the spread of HIV infection** in the Russian Federation.

At the end of December 2020, the Government of the Russian Federation approved the State Strategy for Combating the Spread of HIV Infection in Russia until 2030. The goal of the strategy is to reduce the increase in the incidence of HIV infection from 76,000 cases in 2020 to 45,000 in 2030. A detailed plan for the implementation of this strategy was presented in October 2021, it contains eight thematic units and 29 events. Neither the strategy nor the implementation plan mentions drug pre-exposure prophylaxis. It is important to note that the creation of a system for the prevention of HIV infection is defined as one of the directions of state policy in the field of protecting the health of citizens and demography. The organization of measures to combat HIV infection is regulated by federal law and includes hygienic education of the population, prevention of infection in the provision of medical care and in consumer service organizations, occupational infection, and inter-generational transmission. Also, activities on informing and educating the population have been identified as a priority area of primary prevention. Its implementation is entrusted to AIDS centers, narcological and dermatovenerologic dispensaries, antenatal clinics, and employers.

For the organization of diagnosis and treatment, the Russian clinical guidelines “HIV Infection in Adults”¹⁵ 2020 of the RF Ministry of Health (CG) and the Standard for the provision of primary health care for adults with HIV infection of the RF Ministry of Health (diagnosis, treatment, and follow-up care) are used¹⁶. There are no recommendations on PrEP in these regulations, therefore, doctors cannot rely on them in their prescriptions. In the CG, there are only recommendations for post-exposure prophylaxis. In 2018, the position of the RF Ministry of Health¹⁷ on the possible inclusion of PrEP in prevention programs was expressed in the mass media, but no changes followed. It is important to note that the draft¹⁸ Clinical Guidelines 2020 initially contained a section on pre-exposure prophylaxis with a detailed description of the method application, however this information was not included in the adopted CG.

In 2018, the Specialized Panel of the RF Ministry of Health for the Diagnosis and Treatment of HIV Infection approved recommendations¹⁹ for the introduction and use of PrEP as an important element of prevention among MHSWM in the “Recommendations for the development of a standard

¹⁴ <https://docs.cntd.ru/document/9036485>

¹⁵ HIV Infection in Adults https://cr.minzdrav.gov.ru/schema/79_1

¹⁶ <http://publication.pravo.gov.ru/Document/View/0001202207260029>

¹⁷ Ministry of Health may add anti-HIV drugs to prevention programs

interdepartmental program on HIV prevention in key populations”. Interdepartmental programs should be adopted and implemented in each subject of the Russian Federation. In turn, the analysis of the interdepartmental programs in a number of subjects of the Russian Federation (including those adopted for the period up to 2030) showed that PrEP is not mentioned in the programs and implementation plans.

There are also “National recommendations for the treatment of HIV infection and related diseases, chemoprevention of HIV infection” compiled under the guidance of specialists from the Federal Scientific and Methodological Center for the Prevention and Control of AIDS of the Central Research Institute of Epidemiology of Rospotrebnadzor. They state that indications for pre-exposure prophylaxis for HIV are a high risk of HIV infection and the patient’s willingness to carefully adhere to doctor’s prescriptions for PrEP, including drug regimen and periodic HIV testing. The recommendations have a section on PrEP with a detailed description of all stages of the conduct: counseling, examination before PrEP, regimens of its implementation, observation during PrEP. Taking into account that the recommendations of the RF Ministry of Health and the HIV Treatment Standards are priority in the country, the recommendations of the Federal AIDS Center of Rospotrebnadzor can be used by specialists only as additional educational information.

The section “Prevention of HIV infection” of the Decree²⁰ of the Chief State Sanitary Doctor of the Russian Federation dated January 28, 2021, No. 4 “On approval of sanitary rules and norms SanPiN 3.3686-21 “Sanitary and epidemiological requirements for the prevention of infectious diseases” (as amended on May 25, 2022) states that preventive chemoprophylaxis includes: “pre-exposure prophylaxis with antiretroviral drugs which can be used (as part of certain programs) in non-HIV-infected people at high risk of HIV infection in combination with other preventive measures, including condom use and HIV testing”.

Thus, currently there is no single legislative act regulating the introduction and/or application of PrEP in the Russian Federation. There are scattered references to PrEP in several regulations of various levels and legal significance. Also, PrEP is absent as a means of prevention in the system for combating HIV infection in the federal legislation.

It is important to note that in order to be used in the treatment standards, medicines are assigned an Anatomical Therapeutic Chemical Classification (ATC) code. Tenofovir/emtricitabine has been assigned the ATC code J05AR (Combined Antiviral Drugs for Treatment of HIV Infection), therefore, it cannot currently be used at the state level as a drug for prevention in people without HIV infection. The RF Ministry of Health also approved a nomenclature of medical services with assigning codes that are necessary for payment within the CHI system – as of the time of preparing the report, there is no separate medical service for pre-exposure prophylaxis.

For the introduction and application of any method of prevention, diagnosis, treatment and rehabilitation, as well as for inclusion in clinical guidelines, a clinical testing protocol is required in the Russian Federation²¹. The purpose of clinical testing is the practical application of the method developed and not previously used in the Russian Federation for the treatment of patients with HIV infection. As part of clinical testing, a method can be implemented that is proved to be effective and safe in accordance with the principles of evidence-based medicine. On average, duration of a clinical testing based on which the protocol is prepared is 2–3 years. It is natural to assume that the PrEP method requires compiling of such a protocol, but currently there is no such a protocol.

As part of the study, the official position of the Russian Ministry of Health on PrEP was requested. The response of the department contains data that medical care for patients with HIV infection is provided by healthcare facilities in accordance with clinical guidelines developed by the National Association of Specialists for the Prevention, Diagnosis and Treatment of HIV Infection and the National Virological Association, approved by the Scientific and Practical Council of the Ministry of Health of Russia. At the same time, as mentioned above, the recommendations of the National Association referred to by the Ministry of Health contain clauses about the use of PrEP, while the official Clinical Guidelines of the RF Ministry of Health do not, so even this answer shows contradictions. The response did not contain specific information about the inclusion of the PrEP method in the CG.

To summarize, we can conclude that in terms of legislation, the issue of integrating PrEP into the Russian healthcare system requires multi-level and extensive elaboration.

The registry of Russian clinical trials found no evidence that the study of PrEP was or is being conducted by the Ministry of Health or its subordinate institutions at the state level.

The only agency that studies PrEP in one way or another is Rospotrebnadzor. In scientific journals there is information about the research of the FBIS “Central Research Institute of Epidemiology” of Rospotrebnadzor²². This also can refer to two public procurements mentioning pre-exposure prophylaxis for the supply of the drug tenofovir/emtricitabine for research work on the topic “Studying the efficacy and tolerability of the method of pre-exposure prophylaxis of HIV infection” in 2018²³. Additionally, this was covered in the mass media²⁴, but no published data on this study was found in the public domain.

Currently in Russia, scientific work on the use of PrEP is carried out mainly with the participation of pharmaceutical manufacturers and non-profit organizations working in the field of HIV response. With the support of Pharmasyntez JSC, a study titled “Expanding access to HIV pre-exposure prophylaxis (PrEP) for MHSWM and TGP in Moscow and the Moscow region” was carried out in 2022. At a meeting with the patient community, representatives of Pharmasyntez announced²⁵ that such studies were carried out in Nizhny Novgorod and the Chelyabinsk region.

Registration status of medicines for PrEP in Russia

In Russia, the original Truvada drug was registered at the end of 2011.

Despite repeated and long-term attempts by the patient community to challenge the patent²⁶ for Truvada, the drug is still under a patent protection in the Russian Federation until January 13, 2024.

Despite this, five generics are registered in the Russian Federation. The possibility of applying for the purpose of pre-exposure prophylaxis is specified in the instructions for use for the original Truvada and for all generics registered in the Russian Federation.

²² Federal Budgetary Institution of Science Central Research Institute of Epidemiology of the Federal Service for Supervision of Consumer Protection and Welfare.

²³ <https://itpc-eeca.org/2019/01/25/zakupki-truvady-dlya-dokontaktnej-profilaktiki-v-rf/>

²⁴ Russia began testing pre-exposure prophylaxis for HIV <https://www.interfax.ru/russia/621907>

²⁵ Minutes of the meeting with the pharmaceutical company Pharmasyntez JSC
<https://pereboi.ru/wp-content/uploads/2023/02/Protokol-AO-Farmasintez.pdf>

²⁶ <https://itpc-eeca.org/2020/06/18/farmvestnik-obshhestvennye-organizaczii-osparivayut-patent-na-preparat-truvada/>

Table 2. Registered drugs with INN tenofovir/emtricitabine in the Russian Federation.

Trade name	Manufacturer	Country	Date of registration in the RF
Truvada®	Gilead Science International Limited	UK	29.09.2011
Tenofovir+Emtricitabine	Aurobindo Pharma Ltd	India	29.03.2016
Dokvir	Joint-Stock Company Pharmasyntez (JSC Pharmasyntez)	Russia	06.10.2016
Tenofovir+Emtricitabine VM	Limited Liability Company "Chemical Diversity Research Institute" (LLC "CDRI")	Russia	01.11.2017
NOFORENA®	LLC "Nanopharma Development"	Russia	31.05.2019
Tenofovir+Emtricitabine-KRKA	JSC "KRKA, d.d., Novo Mesto"	Slovenia	05.03.2020

It is important to note that only medicines that have passed the WHO prequalification procedure can be purchased for international programs of the PrEP non-profit sector. The WHO Prequalified Medicines List is used by international purchasing organizations and some governments to manage bulk procurement of medicines. A prequalified drug²⁷ from Aurobindo Pharma Ltd (India) has been registered in Russia.

At the same time, one generic drug, Dokvir, has been sold in pharmacy chains for several years and was even purchased as part of several public [procurements](#). In 2022, the manufacturer created a website dedicated to the promotion of the drug for PrEP²⁸.

The Russian Federation applies a principle of restrictive lists, one of which is the List of Vital and Essential Drugs (VED). When included in this list, the maximum selling price is registered for the drug, after which it can be purchased at the expense of the federal budget. The combination of tenofovir/emtricitabine is not included in the list and can only be purchased at the expense of the budgets of the RF regions, and the price of the drug is dictated by the commercial market.

The last attempt by the Gilead manufacturing company to introduce Truvada into the VED was made in 2017²⁹. However, the maximum price proposed for registration did not satisfy the commission at the RF Ministry of Health - it was considered too high. After that, the company did not resubmit the drug for Vital and Essential Drugs and refused to actively promote this combination in the Russian Federation³⁰. Russian patient organizations have repeatedly called the company to abandon the patent, but so far without any result.³¹ The situation with the sale of generics also remains without a legal assessment from the originating company.

Descovy tenofovir alafenamide/emtricitabine is not registered in the Russian Federation, and the company has no plans to register it.

The combination lamivudine/tenofovir (Cimduo) is undergoing clinical trials for bioequivalence (CT start and end date 24.11.2021-28.12.2023)³².

²⁷ Prequalification of Medical Products <https://clck.ru/33fXw9>

³⁰ Minutes of the meeting between ECAT and Gilead Sciences <https://www.eeca-cat.info/wp-content/uploads/2018/10/Protokol-Gilead-16.10.2019.-Final-1.pdf> p.15

³¹ Patient organizations in Russia called Gilead to abandon patents on Truvada <https://itpc.eeca.org/2020/09/03/pacientskie-organizaczii-v-rossii-prizvali-gilead-otkazatsya-ot-patentov-na-truvad/>

³² Register of Clinical Trials <https://clck.ru/33fY42>

Separate options - lamivudine, tenofovir and emtricitabine in the form of generics - are registered in the Russian Federation in large numbers, all these INNs are included in the Vital and Essential Drug List, but the instructions for them do not contain indications for use as PrEP. It should be added that since September 1, 2022, a new order of the RF Ministry of Health³³ regulating the issues of clinical testing came into force, which provides for the possibility of using off-label drugs if there are references to clinical trials for efficacy and safety or references in leading domestic and/or foreign peer-reviewed scientific journals and publications.

An injectable cabotegravir for PrEP is not registered in Russia as of the time of the report preparation.

Awareness of PrEP in Russia

The 2020 study of the FBIS “Central Research Institute of Epidemiology” of Rospotrebnadzor “Assessment of awareness of HIV-infected patients about the method of pre-exposure prophylaxis, attitudes towards its implementation and prospects for its use in Russia”³⁴ showed that as of the time of the interview, 61% of respondents did not know about the existence of the PrEP method. 16% of respondents with discordant partners noted that they do not use methods to prevent HIV infection. The majority of respondents (77%) expressed a positive attitude towards the PrEP method, 10% reported that they had not thought about it. 47% of respondents assessed PrEP positively, 29% expressed doubt, and 24% assessed it negatively. The main source of information about PrEP for respondents was the Internet, only 8% got to know about the method from healthcare workers.

Another study³⁵ conducted in Russia revealed a low prevalence of PrEP among MHSWM - only 10.8% of all respondents were taking PrEP drugs at the time of the survey or had done so before. Among MHSWM surveyed in Russia, a high level of awareness of PrEP was revealed - 91% of all respondents stated their familiarity with this method of prevention, and 88.8% of respondents would agree to receive drugs for PrEP free of charge, and this may indicate a generally positive attitude of MHSWM to PrEP in the Russian Federation.

At the same time, respondents who refused to receive drugs for PrEP stated the following reasons: doubts about the efficacy of this prevention, lack of information, unwillingness to take drugs on a regular basis, fear of side effects, sex only with a regular partner with a known HIV status. The main reasons for discontinuation of drugs for PrEP are: taking the drug on an as-needed basis, living and having sex only with a regular partner, difficulties in finding drugs at the place of residence.

One of the studies of Rospotrebnadzor, the purpose of which was to analyze the self-assessment of the awareness of healthcare workers, medical students and NPO volunteers of the PrEP method, was conducted in 2021 (174 respondents)³⁶. Survey participants rated their awareness of PrEP issues as average or below average. Therewith, data were obtained on the lack of information on PrEP which hinders the use of the method. Lack of awareness among interviewed healthcare workers, students of medical departments and employees of NPOs is one of the main barriers to the implementation of the PrEP method.

³³ Order of the Ministry of Health of Russia No. 103n dated February 22, 2022 “On approval of the procedure for developing standards of medical care”

³⁶ INFECTOLOGY JOURNAL Official publication of the Interregional Public Organization “Association of Infectious Disease Doctors of Saint Petersburg and the Leningrad Region” Editor-in-Chief Academician of the Russian Academy of Sciences Yu.V. Lobzin. Appendix 1 Volume 13, No. 3, 2021 p.131 (Journal website <https://journal.niidi.ru/jofin>)

Another study by the Central Research Institute of Epidemiology of Rospotrebnadzor³⁷ on the awareness of specialists of the method of pre-exposure prophylaxis of HIV infection and the willingness to recommend it showed insufficient awareness of the survey participants of the PrEP method which leads to a low willingness to recommend the PrEP method to patients. Taking into account that 93.2% of the survey participants have experience of working with HIV-infected patients, the task of informing specialists about the PrEP method seems to be relevant.

A study by the Central Research Institute of Epidemiology of Rospotrebnadzor and the Regional Charitable Public AIDS Foundation “SHAGI” (Moscow) titled “Assessment of awareness of volunteers of the ways to prevent HIV infection, including the method of pre-exposure prophylaxis (PrEP)”³⁸ showed the lack of knowledge about prevention methods, including the method of PrEP among the volunteers of the organization involved in HIV-infection prevention.

Similar findings about lack of knowledge have been found in studies on PrEP among people who inject drugs³⁹.

Another study, “Risks, Resources, and Prospects for PrEP: Results from a Survey of Healthcare Workers”, found that respondents considered the lack of information coupled with low accessibility to be the main barrier to promoting PrEP. With a positive assessment of the prospects for PrEP, the respondents considered the main precondition for practical application of the method to be an increase in access, including through state funding of the program for pre-exposure prophylaxis of HIV infection⁴⁰.

In the Russian Federation, there is an urgent need of measures to raise awareness of PrEP as an effective prevention measure among potential recipients of the service, medical specialists, general practitioners, as well as NPO workers and volunteers involved in HIV prevention.

Analysis of search engines shows not too high, but steady interest in pre-exposure prophylaxis.

The image shows two screenshots of search engine results. The left screenshot is for the search term 'доконтактная профилактика' (PrEP) and shows 341 results in a month. The right screenshot is for 'ДКП ВИЧ' (PrEP) and shows 728 results in a month. Both screenshots include a table of search statistics.

Статистика по словам	Показов в месяц
доконтактная профилактика	341
доконтактная профилактика вич	208
препараты доконтактной профилактики	58
доконтактная профилактика вич препараты	51
доконтактная профилактика купить	36
доконтактная профилактика вич купить	27
доконтактная профилактика вич препараты купить	18
доквир доконтактная профилактика	16

Статистика по словам	Показов в месяц
дкп вич	728
+что значит дкп вич	42
дкп вич препараты	40
дкп вич купить	27
вич отрицательный дкп +что +это	27
вич отрицательный дкп +что +это значит	16
схема дкп вич	12
дкп вич статус	11

³⁷ Ibid, p. 143

³⁸ Ibid, p. 144

³⁹ INFECTOLOGY JOURNAL Official publication of the Interregional Public Organization “Association of Infectious Disease Doctors of Saint Petersburg and the Leningrad Region” Editor-in-Chief Academician of the Russian Academy of Sciences Yu.V. LOBZIN. APPENDIX 1 Volume 13, No. 3, 2021, p. 168

⁴⁰ Ibid, p. 145

Figure 3. Number of queries in the Yandex search network per month.

Here, Moscow accounts for most of the queries, Saint Petersburg is in the second place, and Ekaterinburg is in the third one.

In terms of the number of queries during 2022, the peak was in the summer months.

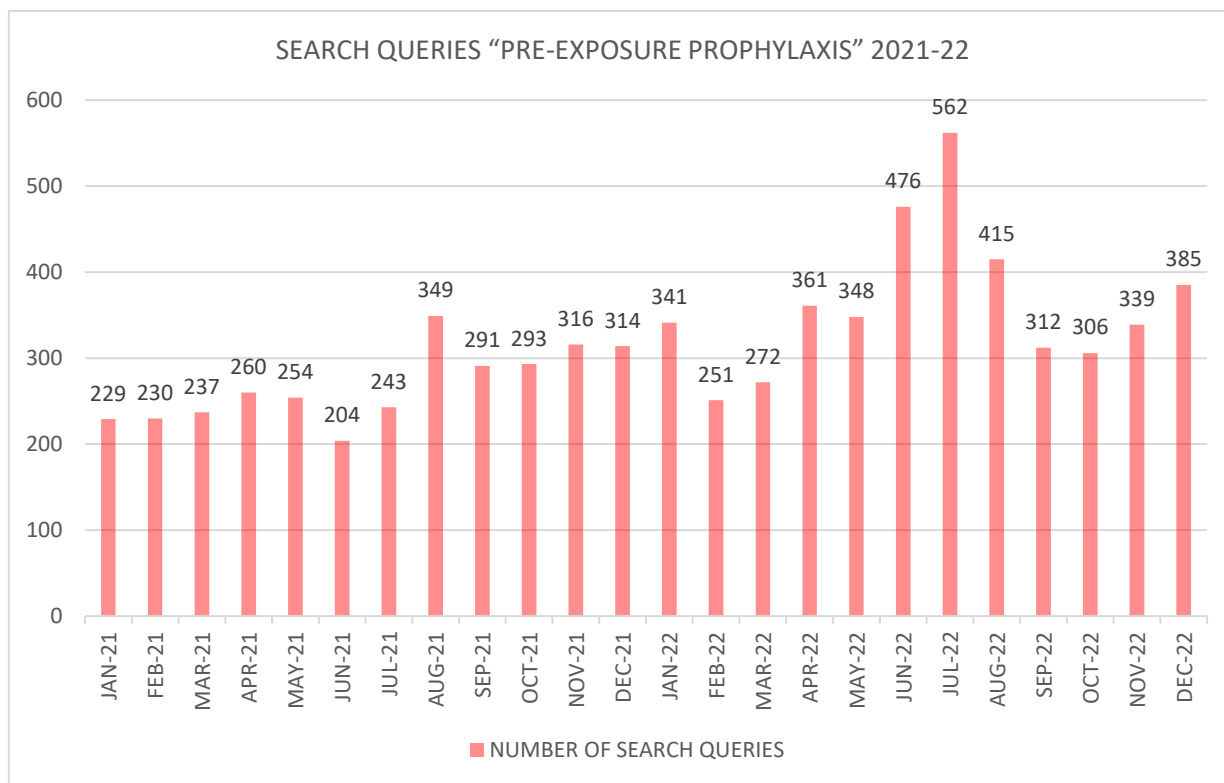


Figure 4. Number of search queries for the phrase “Pre-exposure prophylaxis” in the Yandex search engine 2021-22

Thus, we can conclude that there is a stable demand for information about pre-exposure data, albeit small.

Availability of PrEP in Russia

The only official data that mention PrEP is the analytical report “Results of the Rospotrebnadzor study on the causes of deaths in patients with HIV infection in the Russian Federation in 2019-2021”.⁴¹ The report states that data have been obtained on the limited use of the pre-exposure prophylaxis method in Russia. In 2019, only 10, in 2020 - 17, in 2021 - 37 people received PrEP in the country.

In the Russian Federation, there are few programs for access to PrEP which are implemented by non-profit organizations operating in the field of HIV response. However, as a rule, these programs are very limited in terms of the number of participants. For example, 100 people were supposed to participate in the 2022 program⁴² of the AIDS.CENTER Foundation.

⁴¹ The report was prepared by V.V. Pokrovsky, N.N. Ladnaya, A.V. Kravchenko, N.V. Kozyrina, E.V. Sokolova, O.G. Yurin, D.G. Chekryzhova, Specialized research department for the prevention and control of AIDS of the Central Research Institute of Epidemiology of Rospotrebnadzor on the basis of data obtained from the territorial centers for the prevention and control of AIDS and the territorial departments of the Federal Service for Supervision of Consumer Protection and Welfare.

⁴² “AIDS.CENTER” will provide 100 people with free pre-exposure prophylaxis of HIV for a year

PrEP websites from NPOs⁴³ operating in the field of HIV response are available on the Internet. However, the number of Russian-language websites on PrEP is insignificant compared to the international segment.

Basically, people can buy drugs in pharmacies on their own. However, there are barriers to overcome here as well. The drugs are dispensed in pharmacies only by prescription. It should be noted that the structure of assistance to PLH in the Russian Federation is organized as a system of special medical facilities in each subject of the Russian Federation - Centers for Fight against AIDS and IDs. A patient with HIV gets registered at the dispensary, visits an infectious disease specialist, various specialists, and regularly receives ARV drugs for the treatment of HIV infection free of charge. Thus, based on the current legislation, a person who obviously does not have an HIV diagnosis cannot, on a permanent basis, receive free consultations from an infectious disease specialist or another specialist, take the necessary tests and receive PrEP and prescriptions for PrEP at the state AIDS center.

Citizens of the Russian Federation can receive medical services within the framework of compulsory medical insurance in polyclinics. An HIV test can be taken free of charge subject to a referral from an infectious disease specialist or therapist. However, there is no data on whether PrEP counseling and drug prescriptions can be obtained within the primary care system. There is also no reason to believe that currently there are any plans and resources to involve healthcare workers in HIV prevention in the outpatient care structure.

There is an alternative in the form of for-profit private clinics, however, most likely, not everyone can pay for expensive services. Furthermore, such clinics mainly operate in large cities.

Drugs for the treatment of HIV infection are procured by the state under the public procurement mechanism. The main part is purchased centrally at the expense of the federal budget. In the RF subjects, drugs can be purchased additionally at the expense of the regional budgets. In 2021-22 tenofovir/emtricitabine FDC appeared in the regional public procurement, but given that PrEP is not implemented at the state level, these ARVDs are most likely purchased for HIV treatment, and even in this case their volume is insignificant.

It should be noted that ARV drugs, including tenofovir/emtricitabine, lamivudine, tenofovir and emtricitabine, are sold only in a limited number of pharmacies in major cities. At the same time, their cost is often much [higher](#) than in the public procurement segment.

Given the potential difficulties in obtaining consultation by a specialist and the current practice of pharmacies selling prescription drugs without a prescription, it is likely that in terms of PrEP people are left to themselves, and in practice may take drugs without supervision. This may affect the adherence to and efficacy of PrEP.

Analysis of the commercial PrEP market in the Russian Federation

An analysis of the Yandex search engine in terms of a query to purchase drugs for PrEP showed a stable monthly demand for these drugs, with some increase by the end of 2022. Since mid-2021, the generic drug Dokvir has become the dominant drug in queries.

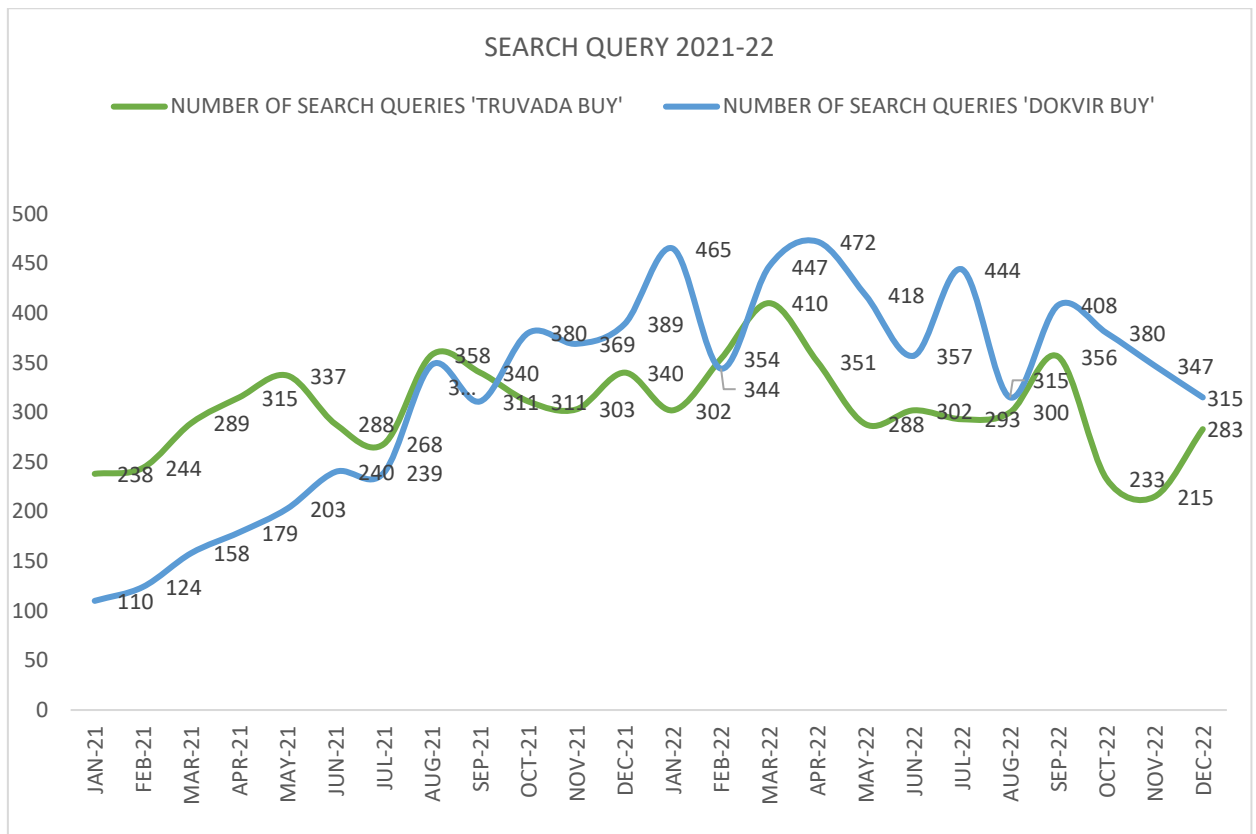


Figure 5. Yandex search queries for PrEP drugs by month (2021-22)

Given a number of key factors, further analysis of PrEP availability in terms of prices and demand will only be conducted for the tenofovir/emtricitabine combination. Analysis of the availability of monads tenofovir and emtricitabine or lamivudine as PrEP was not performed because tenofovir and lamivudine are the most popular NRTI combinations used in HIV regimens.

In addition, given that there are more affordable options for HIV treatment, the authors of the report suggest that the bulk of tenofovir/emtricitabine sold through pharmacy chains, private clinics and non-profit organizations is purchased for PrEP.

[DSM Group](#) data were used to analyze the availability of PrEP in the commercial pharmacy market. DSM Group data is based on an analysis of purchases across the entire commercial pharmaceutical market in Russia, inter alia taking into account sales on orders on online booking websites. The data reflect directly sales in pharmacies, and not deliveries to pharmacies or orders on online platforms. It is important to note that the figures do not include drug sales in for-profit private clinics. Thus, the analysis below does not accurately describe the volume of PrEP purchases, but it can show the general trend and the approximate extent of PrEP popularity in the commercial market.

Commercial procurement analysis period: September 2021 - September 2022

Regions: the whole Russia (as of September 2022)

DSM Group methodology.

Total procurement volume

As part of the analysis, 2 tenofovir/emtricitabine drugs were considered - TN Truvada (original) and TN Dokvir (generic).

According to DSM Group, tenofovir/emtricitabine combination was purchased in retail pharmacy chains in the amount of 1766 packages in total for the period September 2021 - September 2022. On average, 135 packages were purchased monthly, regardless of the TN. At the same time, a slight

increase in purchases in 2022 is recorded. The average number of packages per month in 2021 is 85, in 2022 it is 158.

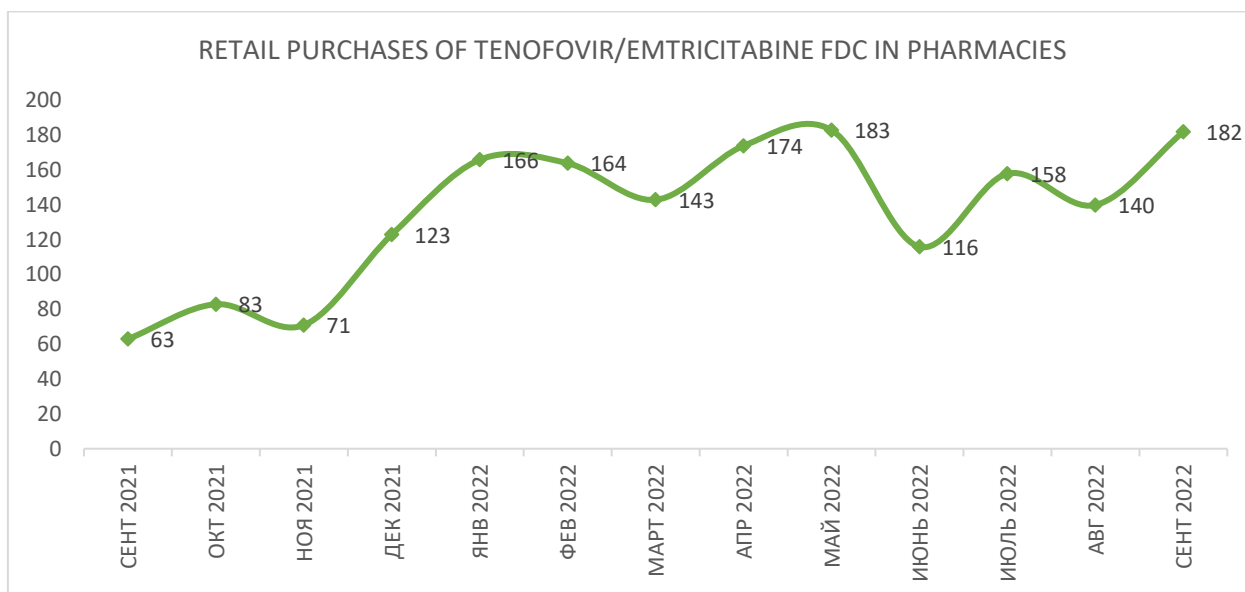


Figure 6. Purchase volumes of tenofovir/emtricitabine by months (packages)

Based on the recommended maximum drug regimen for PrEP purposes (daily once a day, 365 days a year), the volume purchased for the incomplete year 2022 is 109 one-year courses, and in total for the period September 2021-September 2022 - 135 courses (it is important to note that the calculation is based on the assumption of long-term adherence to the drug, the actual number of people taking PrEP may be significantly higher).

Despite the significant difference in price between generic Dokvir and the original drug Truvada, almost the entire volume of purchases through pharmacy chains falls on Truvada - 85% (1515 packs). The drug Dokvir has been actively bought through pharmacy chains since October 2021. According to DSM Group, during the analyzed period, 251 packages of generic tenofovir/emtricitabine (15%) were purchased through pharmacy chains.

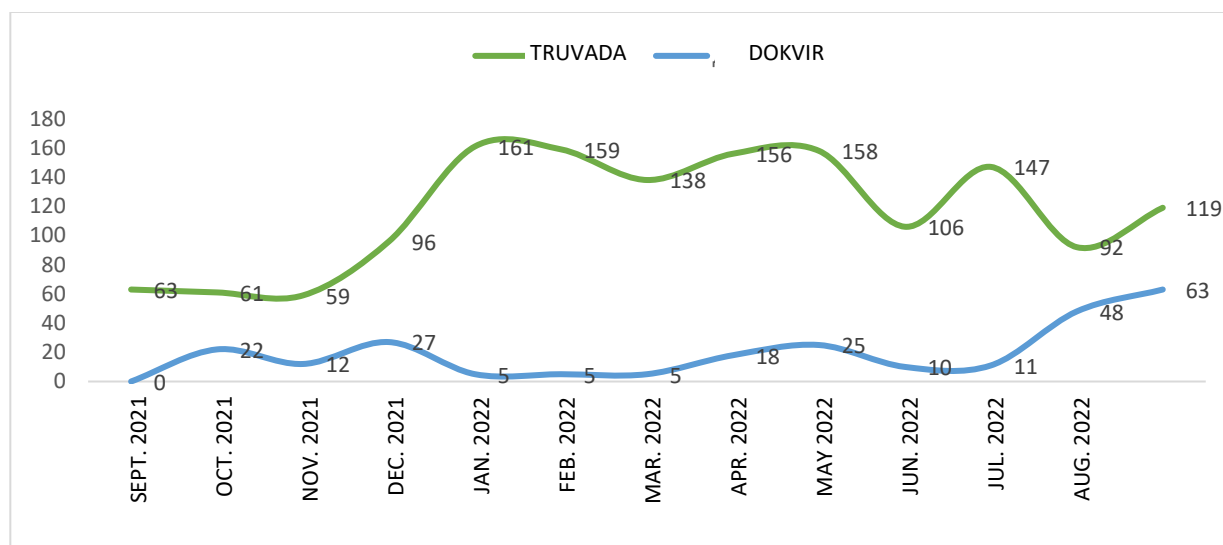


Figure 7. Volumes of Truvada and Dokvir in packages by months according to DSM Group/

The amount of money spent on tenofovir/emtricitabine amounted to 25,502,561 rubles. Truvada accounted for 25,078,117 rubles (98% of the total amount of tenofovir/emtricitabine sold in pharmacy chains), Dokvir - for 424,444 rubles.

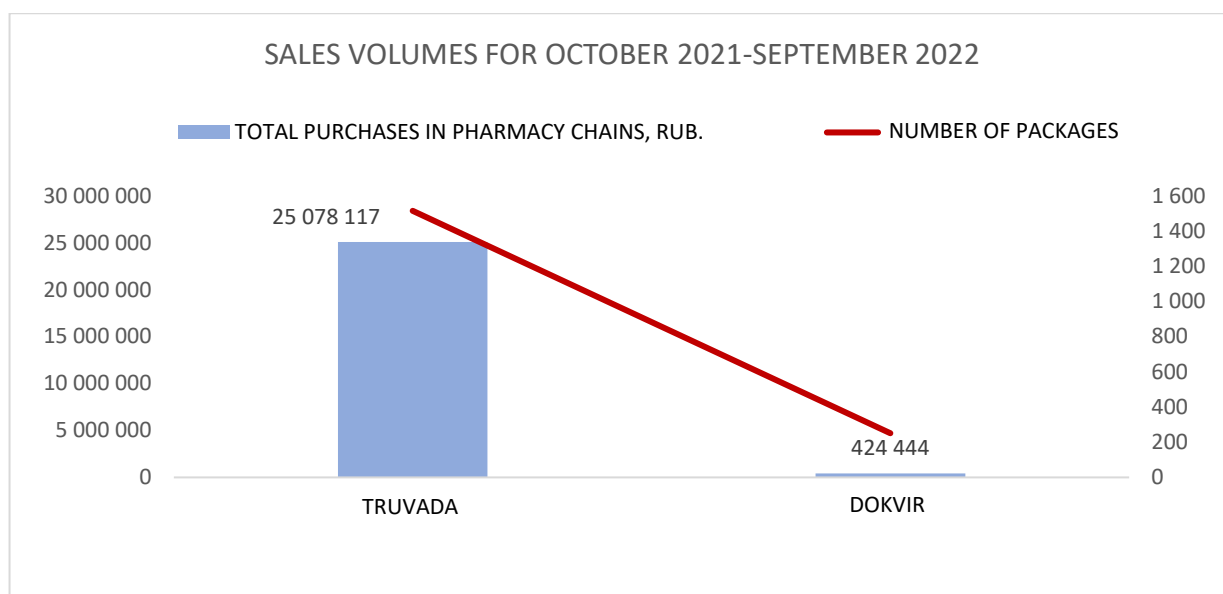


Figure 8. Tenofovir/emtricitabine volume-to-cost ratio by TN.

The cost of a Truvada package in retail pharmacy chains averages ~15,000 rubles (\$217⁴⁴). The cost of the one-year course* is 180 thousand rubles (\$2610)^{**}. The average cost of a generic is 1,680 rubles per package (\$24), the cost for a year is 20,000 rubles (\$294). That is, the generic is **almost 9 times** cheaper than the original, which in the future could increase the use of the drug as part of pre-exposure prophylaxis. However, it is important to note that at a meeting with patients Pharmasintez announced⁴⁵ that in 2022 a decision was made to stop marketing activities and minimize all marketing expenses. In fact, the generic entered the commercial market at the end of 2021, and in 2022 the marketing campaign for its promotion by the manufacturer is likely to be suspended. According to the manufacturer, currently there are 25 pharmacies in major cities where regional commercial managers work who visit AIDS Centers and inform specialists about the pharmacies where the drugs can be bought. In 2022, the manufacturer of the original, the Gilead company, also decided to limit its activities in the territory of the Russian Federation and suspend non-core business operations⁴⁶. In this context, there is a risk that given the low awareness among medical staff and patients, the knowledge about the drug as a PrEP method will remain low, and purchase volumes will remain at the level of 2021-2022 at best.

Table 3. Weighted average cost of tenofovir/emtricitabine by TN in commercial retail pharmacies, Oct. 2021-Sept. 2022

TN	Truvada	Dokvir	Difference, times
Weighted average cost of a package	14,900 RUR	1,680 RUR	~9 times
Weighted average cost of a one-year course	178,800 RUR	20,160 RUR	

The cost of drugs **not** in pharmacy chains varies quite widely depending on the method of selling. Figure 9 shows data on the cost of drugs in different segments of the pharmaceutical market with different trade names and in various combinations (excluding retail commercial pharmacies). Public

⁴⁴ Yearly average exchange rate in 2022 for \$1 is 68,487 rubles

⁴⁵ Minutes of the meeting with the pharmaceutical company Pharmasintez JSC, page 11 <https://pereboi.ru/wp-content/uploads/2023/02/Protokol-AO-Farmasintez.pdf>

⁴⁶ Minutes of the meeting with the pharmaceutical company Gilead <https://pereboi.ru/wp-content/uploads/2023/02/Protokol-Gilead.pdf>

procurement costs are provided to illustrate the price level for tenofovir/lamivudine in combination and alone.

	Chain pharmacies	Private clinic (Moscow)	Private clinic (St. Petersburg)	Government procurement
Truvada	14900	15500	16500	12339
Dokvir	1680	2000	2450	1379
Tenofovir + emtricitabine (as mono-drugs)	2370	920	1005	497
Tenofovir + lamivudine (as mono-drugs)	1550	1620	1965	887

Created with Datawrapper

*TN Tenofovir, Tenof, Amiviren, Emtritab.

**Minimum prices Ministry of Health - tenofovir+lamivudine;

Weighted average prices Subjects of the Russian Federation - tenofovir/emtricitabine, tenofovir, emtricitabine.

Figure 9. Cost of PrEP regimens in rubles for 1 month (prices as of January 2023) in rubles per package in various market segments.

Tenofovir/emtricitabine (as a combination) was purchased in 14 regions of Russia. The vast majority of drug sales fell on Moscow - 71% of the total volume of packages sold through pharmacy chains, of which Truvada accounted for almost the entire volume - 97%. Almost the entire remaining total volume (24%) fell on three other regions - Omsk Region, the Republic of Sakha (Yakutia) and Perm Territory. At the same time, it is important to note that the Russian Federation uses the List of the minimum range of drugs required for the provision of medical care⁴⁷ that does not include tenofovir/emtricitabine, which complicates access to the drug in the regions of Russia.

The website of the generic manufacturer lists 21 regions where the drug is supposed to be available in pharmacies. At the same time, it is difficult to confirm whether it can really be found in these regions and pharmacies. However, even this information is sufficient to estimate regional coverage: the drug is potentially available only in a number of regions, and only in major cities. Accordingly, it is premature to talk about wide access to the drug.

The generic manufacturer also informed that doctors do not issue prescriptions and do not want to send patients to pharmacies referring to the law on free provision of drugs for HIV treatment, and those, in turn, do not stock tenofovir/emtricitabine, as it is not in demand in the volumes which they are accustomed to.

An analysis of the availability of the drug in pharmacies showed that in Moscow and Saint Petersburg the original and generic can be bought even in network pharmacies. In other regions, availability is limited. In the vast majority of regions, the drug is mainly available only in online pharmacies with delivery to the region. The search was carried out on the Internet for each subject with the help of pharmacy and medical services aggregators [Spravmedika](#) and [Pharmindex](#).

Table 4. Availability of drugs for PrEP in pharmacies in the regions according to an Internet query.

RF Subject	Availability in pharmacies	
	Truvada	Dokvir
Irkutsk Region	–	–
Krasnoyarsk Territory	–	+
Novosibirsk Region	–	+
Orenburg Region	–	–
Perm Territory	–	+
Samara Region	–	+

Saint Petersburg	+	+
Sverdlovsk Region	-	+
Tomsk Region	-	+
Tyumen Region	-	+
Chelyabinsk Region	upon request	+

As part of the study, requests were sent to the manufacturers of TN Truvada (Gilead Sciences) and TN Dokvir (JSC Pharmasyntez) on the sold volume of the drug tenofovir/emtricitabine, but both companies refused to provide data, citing trade secrets.

According to the data obtained from unofficial sources, in 2022 manufacturers shipped to the commercial sector at least 2,000 packages of TN Truvada and more than 6,000 packages of TN Dokvir which may indirectly indicate a higher demand for generics than is recorded in available pharmacy chain data. It is important to take into account that drugs can be sold not only through pharmacy chains and platforms, but also within the projects of non-profit organizations and private clinics that are not included in the DSM Group database methodology.

Consequently, the availability of tenofovir/emtricitabine in the pharmacy segment is very limited. The drug can be purchased only in major cities, in online pharmacies subject to the availability of a pick-up point in the locality. The limited supply in pharmacies is due to both the absence of the drug in the mandatory assortment minimum of pharmacies and the need for a prescription for the drug, and the lack of demand is due to low motivation to use PrEP.

Considering the available data from DSM Group, we can only emphasize the trends: TN Dokvir, having entered the market with a price almost 10 times lower than the original, is potentially a very popular drug, but it is practically not sold through pharmacy chains, unlike Truvada.

Conclusions

Existing international guidelines consider PrEP as part of a comprehensive system of HIV prevention interventions, paying particular attention to the HIV key populations.

Drugs approved for PrEP have been proved to be safe and effective in a number of international studies, provided that PrEP is conducted under medical supervision with mandatory periodic HIV testing. The list of drugs approved for PrEP is constantly expanding in international guidelines.

In Russia, there is virtually no access to pre-exposure prophylaxis for HIV. The practice of applying the PrEP method in the Russian Federation is very limited which is due to a complex of reasons.

Currently there is no single legislative act regulating the introduction and/or application of PrEP in the Russian Federation. There are only scattered references to PrEP in several regulations of various levels and legal significance. Also, PrEP is absent as a means of prevention in the system for combating HIV infection in the federal legislation. In terms of legislation, the issue of integrating PrEP into the Russian healthcare system requires multi-level and extensive elaboration.

The lack of a formed-up system of HIV prevention at the level of primary health care for the general population, including representatives of the key groups, does not allow receiving assistance in obtaining and using PrEP in ordinary medical facilities. At the same time, specialized ID institutions mainly provide assistance to people living with HIV.

A number of studies conducted in Russia have shown that the level of knowledge about PrEP is low in the country and there is an urgent need of measures to raise awareness of PrEP both among

potential recipients of the service, and among medical specialists, general practitioners, and NPO workers, volunteers involved in prevention of HIV infection.

Analysis of search engines shows insignificant, but steady interest in pre-exposure prophylaxis. However, at the same time, the availability of drugs in the pharmacy segment is very limited. The drug can be purchased only in major cities, as well as on order in online pharmacies, subject to the availability of a pick-up point in the locality and a prescription issued by a medical specialist.

The uncertain status of ARV drugs particularly in terms of their use specifically for PrEP and the absence of HIV prevention recommendations are a significant barrier both to the purchase of drugs for PrEP at the state level, and to recommendations by medical specialists and self-purchase in pharmacies.

The analysis of commercial pharmacies sales showed an insignificant sales volume of drugs for PrEP in the Russian Federation. In total, for the period October 2021-September 2022, PrEP was purchased in 14 subjects of the Russian Federation. Also, the data show that the main volume fell on Moscow (71%), and three other regions - the Omsk Region, the Republic of Sakha (Yakutia) and the Perm Territory (24%).

The vast majority of sales for the analyzed period fell on the original Truvada - 97%. The amount of money spent on tenofovir/emtricitabine amounted to 25.5 mln rubles. Truvada accounted for 25 mln rubles, for Dokvir - 424 thousand rubles (data from DSM Group).

The cost of a Truvada package averages 15 thousand rubles. The cost of the one-year course is 180 thousand rubles. The average cost of a generic is 1680 rubles per package, the cost for a year is 20 thousand rubles. In fact, the generic is almost 9 times cheaper than the original, but the latter has an uncertain legal status with a valid patent for the original. At the same time, there is evidence of the sale of drugs for PrEP not only through pharmacy chains, but also through NPO projects and private clinics. The volume of the drugs use may differ from the data of the pharmacy chains analysis, while talking about the large-scale use of PrEP is premature, even taking into account the sale of drugs through other channels, and not just pharmacy chains.

The tenofovir/emtricitabine combination is protected by a patent in Russia until January 2024, despite many years of efforts by non-profit organizations to challenge the patent and call the patent holder to ensure conditions for large-scale access to this drug in the Russian Federation.

Recommendations

The use of PrEP should be considered as part of an overall zero-risk infection strategy in conjunction with evidence-based treatment as prevention, rapid start of ART, pre-exposure prophylaxis, and post-exposure prophylaxis.

There are two parallel directions to be considered in the issue of PrEP introduction: **expanding access to PrEP at the commercial level and access to PrEP as part of free public provision, similar to HIV medicines.**

In order to expand accessibility in the commercial sector, large-scale introduction of affordable generic options is needed. Given the current patent for Truvada and the availability of generics in the market, this requires the following steps from Gilead: a multiple reduction in the price of Truvada; official refusal to prosecute generic companies, or the issuance of a voluntary license to manufacturers, or an official refusal to exercise intellectual property rights to the drug (the so-called non-enforcement letter).

PrEP as a method of prevention should be included in federal HIV programs in the Russian Federation. It is necessary to unify the legal framework regarding the application of the PrEP. It is critical that PrEP be included in new clinical guidelines for HIV prevention and treatment.

It is necessary to include the drug tenofovir/emtricitabine in the restrictive lists, mainly in the List of Vital and Essential Drugs and the pharmacy assortment minimum.

It is extremely important to regularly implement educational projects to raise awareness of the PrEP method among all participants of the process (volunteers, doctors, NPO workers, representatives of the key groups, the general population, representatives of the pharmacy business, decision makers, etc.).

Patient community organizations and non-profit organizations operating in the field of HIV and having a medical license are encouraged to initiate projects to provide PrEP to representatives of the key populations.

Appendix 1. Draft clinical guidelines for the use of PrEP in Russia 2020 (this section was not adopted and is not included in the current CG)

The indications for pre-exposure prophylaxis of HIV infection are a high risk of HIV infection and the patient's willingness to carefully adhere to doctor's prescriptions for PrEP, including drug regimen and periodic HIV testing. The WHO recommends PrEP if the HIV prevalence in the patient's risk group is 3% or more".

Groups	PrEP recommended
MHSWM	+/-
TGP	+/-
CSW	+/-
PWUD	+/-
Uninfected partners of patients with HIV infection (who have not achieved viral suppression)	+/-
Sexually active heterosexual persons at high risk of infection (large number of partners, irregular condom use), including:	-
with a recent STD infection	-
with recent contact for HIV post-exposure prophylaxis	-
having sex while under the influence of drugs	-
Prisoners	-

In the table, the categories are marked with a "+/-" sign, since depending on the specific situation they may or may not be included in the target groups.

A contraindication to PrEP is the presence of HIV infection, as well as clinical and laboratory signs suggesting acute HIV infection, creatinine clearance less than 60 ml/min, intolerance to drugs for PrEP.

PrEP implementation

Before the start of PrEP, it is recommended to assess the features of risky behavior, the presence of motivation to take a course of pre-exposure prophylaxis using the motivational interview method.

Before the start of PrEP, the patient is consulted and informed:

- of the goals and principle of PrEP, its efficacy, role in a set of measures aimed at preventing HIV infection;
- of the principle of voluntary participation in the pre-exposure prophylaxis program;
- that the drug should be taken by the patient strictly in accordance with the doctor's recommendations;
- of methods of preventing HIV infection, including measures aimed at reducing the risk of exposure to HIV. That the use of condoms and lubricants increases the efficacy of PrEP, additionally reducing the risk of sexual transmission of HIV;
- of the need to apply measures aimed at preventing other STIs and diseases transmitted through blood, including barrier methods, measures of protection against unwanted pregnancy;
- of the regimen of taking the drugs used;
- of possible side effects and actions in case of their occurrence. The most common side effects with TDF are nausea and flatulence, with FTC - rash and headache. Also, the patient should be informed of the infrequent but significant side effects of TDF - nephrotoxicity and effects on mineral metabolism;
- of possible drug interactions of the drugs used for PrEP, in particular of the possible summation of the toxic effect when combined with other nephrotoxic drugs (in particular, some antiherpetic drugs and those used in the treatment of hepatitis C);
- of the need for regular medical supervision.

Examination before starting PrEP

Pre-PrEP screening should ensure that the participant is not infected with HIV and assess whether there are any contraindications or restrictions to prescribing drugs intended for PrEP. In particular, TDF and FTC suppress the multiplication of not only HIV, but also the hepatitis B virus, therefore, in the presence of this infection, their administration with subsequent cancellation can exacerbate the course of the disease. The presence of chronic hepatitis B is not a contraindication to PrEP, but the presence of hepatitis should be taken into account when it is administered or discontinued in such patients. In addition, TDF can have a nephrotoxic effect (its administration at creatinine clearance less than 60 ml/min is contraindicated) and affect mineral metabolism, in particular, bone calcification, which is especially significant for elderly women. It is also recommended to conduct a study on the presence of diseases that are often found in patients at high risk of contracting HIV (hepatitis B and C, STIs).

The patient should be informed that taking drugs for PrEP may not provide an immediate preventive effect. Within seven days after the start of PrEP, there is an increase in the drug concentration in the tissues to a level that provides the maximum preventive effect.

People may consider stopping PrEP if they are no longer at high risk of HIV infection. However, it is recommended to stop taking PrEP no earlier than 28 days after the last risky exposure that could lead to the risk of HIV infection, this will preserve its protective effect.

Voluntary informed consent of the participant is required to participate in the pre-exposure prophylaxis program.

The following testing is recommended:

Consultation with an infectious disease specialist (in addition to consulting the participant, attention should be paid to the signs of acute HIV infection and symptoms of STIs when taking history and performing physical examination). If necessary, consultation with other specialists.

A test for antibodies to HIV in the blood (preferably with test systems that also detect the p24 antigen). The test result should be not older than 1 week. The use of detection of antibodies in saliva for this purpose is not recommended due to the possible lower sensitivity.

Examination of kidney function (general urinalysis, determination of creatinine in the blood and calculation of creatinine clearance). If creatinine clearance is less than 60 ml/min, TDF, and therefore PrEP, is contraindicated.

Testing for hepatitis B (test for HBsAg and anti-HBc total). If a positive result is detected, further actions should be carried out that are determined by the algorithm for diagnosing hepatitis B.

HCV antibody test.

Serological testing for syphilis.

Pregnancy test for women.

PrEP regimens

The following regimens can be used for PrEP:

TDF 300 mg + FTC 200 mg once a day.

TDF/FTC in the form of a combination drug with a fixed dose combination - once a day.

TDF - 300 mg once a day (this regimen shows less efficacy with equal safety and therefore can only be considered as acceptable).

It should be taken into account that the instructions approved in Russia for the use of these drugs indicate the possibility of using for the prevention of HIV infection only for the TDF/FTC drug in the form of a combination drug with FDC. The use of other regimens would constitute an off-label prescription and the patient should be informed thereof.

Supervision during PrEP

The goal is to counsel the patient on HIV prevention, determine the patient's HIV status, form and assess adherence, detect and correct side effects, and identify possible concomitant diseases, including viral hepatitis and STIs.

Recommended examinations:

Consultation with an infectious disease specialist - 1 and 3 months after the start of PrEP, then every 3 months. During the consultations, special attention should be paid to signs that make it possible to suspect the presence of acute HIV infection and STIs. If necessary, appointment of consultations with other specialists.

Test for HIV antibodies - 1 and 3 months after the start of PrEP, then every 3 months.

Pregnancy test for women who may become pregnant - every 3 months.

Creatinine test and creatinine clearance calculation at 3 and 6 months, then every 6 months. In diseases accompanied by impaired renal function (for example, diabetes mellitus, hypertension), this testing should be carried out more often. If creatinine clearance is less than 60 ml/min, PrEP should be discontinued. If creatinine clearance is reduced, but has not reached this level, consultation with a nephrologist is recommended, and the decision to continue PrEP should be made on an individual basis.

Serological tests for hepatitis B and C, syphilis - every 6 months.

Although TDF negatively affects bone mineralization, special tests for mineral metabolism, in particular DEXA scanning, are not recommended during PrEP. However, the issue of their

appropriateness may arise with long-term (more than one year) PrEP or in patients with an increased risk of osteoporosis.

Upon 12 months of PrEP, it is recommended to discuss the appropriateness of its continuation with the patient. If PrEP is discontinued for any reason and at any time during PrEP, it is recommended that the patient be tested for HIV. Counseling on HIV prevention is also provided.

Appendix 2. Cost of PrEP regimens in rubles for 1 month (prices as of January 2023) in rubles per package

Drug/regimen	SRM (maximum selling price)	Private clinic (Moscow)	Private clinic (Saint Petersburg)	Public procurement**
Truvada	–	15,500	16,500	12,339
Dokvir	–	2,000	2,450	1,379
Tenofovir + lamivudine (as monads)*	3,597	920	1,005	497
Tenofovir+emtricitabine (as monads)*	1,634	1,620	1,965	887

*TN Tenofovir, Tenof, Amiviren, Emtritaб.

**Minimum prices Ministry of Health - tenofovir+lamivudine;

Weighted average prices Subjects of the Russian Federation - tenofovir/emtricitabine, tenofovir, emtricitabine.