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ANTIRETROVIRAL DRUGS PROCUREMENTS TO ADDRESS HIV/AIDS TREATMENT AND DRUGS PROCUREMENTS TO ADDRESS VIRAL HEPATITIS C TREATMENT IN THE REPUBLIC OF KAZAKHSTAN FULL STUDY REPORT FOR THE YEAR 2018

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АНТИГЕПАТИТ'С
AGEP'C

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AUTHORS AND ACKNOWLEDGEMENTS

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The references made to any treatment regimen in this report should, under no circumstances, be taken as an alternative to consulting with a licensed medical specialist.

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ABBREVIATIONS

TDF	Tenofovir Disuproxil Fumarate
FTC	Emtricitabine
EFV	Efavirenz
ARV, ART	Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
WHO	World Health Organization
SFMA	Statutory Free Medical Assistance
II	Integrase Inhibitor
PI	Protease Inhibitor
PLHIV	People Living with HIV
MHSP	Ministry of Health and Social Protection of the Republic of Kazakhstan
INN	International Non-Proprietary Name
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NtRTI	Nucleotide Reverse Transcriptase Inhibitors
NNRTI	Non Nucleoside Reverse Transcriptase Inhibitor
TN	Tradename
RoK	Republic of Kazakhstan
CSHI	Compulsory Social Health Insurance
AIDS	Acquired Immune Deficiency Syndrome
CMIF	Compulsory Medical Insurance Fund
VHC	Viral hepatitis C
MH RoK	Ministry of Health of the Republic of Kazakhstan
SKO	South Kazakhstan region
RDC	Research and development centre
MNE RoK	Ministry of National Economy of the Republic of Kazakhstan
MP MKRoK	Medical products of the Ministry of Health of the Republic of Kazakhstan
MP	Medicinal products, drugs
ATC	Anatomical Therapeutic Chemical Classification System
KNDF	Kazakhstan National Drug Formulary
AT	Antiviral therapy
HC	Hepatic cirrhosis
LED	Ledipasvir
SOF	Sofosbuvir
OMB/PAR/ RIT+DAS1	combination of ombitasvir, paritaprevir, ritonavr + dasabuvir
VEL	velpatasvir
RBV	ribavirin
EBR/GZR	fixed combination of elbasvir and grazoprevir
SMV	simeprevir
Peg-IFNα	pegylated interferon
DCV	daclatasvir
UNDP	United Nations Development Program
SD	Single distributor
PC MH RoK	Pharmacy Committee of the Ministry of Health of the Republic of Kazakhstan
DH	Department of Health
REHC	Republican e-health center
EG	Evidence grade

GLOSSARY:

Intellectual property is a concept that includes the rights governing relations that develop in the process of creating, sharing and using intellectual products. In other words, intellectual property represents exclusive rights to the results of intellectual and creative activity:

Exclusive right is the right of patent owner to use the industrial property in any way at its discretion;

Intellectual property asset is a category of property that includes intangible intellectual deliverables and intellectual property designations of parties to the civil transactions, goods, works and services;

Patentability requirements are the conditions for granting legal protection to industrial property.

RESEARCH SUMMARY

This study contains detailed data on the procurement of ARV drugs and antiviral medications for the treatment of hepatitis C virus for 2018, indicating types of procurement, the mechanisms, and suppliers used. Also, epidemiological data and information on legislation in force in 2018 are provided herein. The key trends in price changes, statutory acts and treatment regimens in comparison with 2017 were analyzed and presented.

Study on procurement of antiretroviral medicines for the treatment of HIV infection

Key Findings According to the Report:

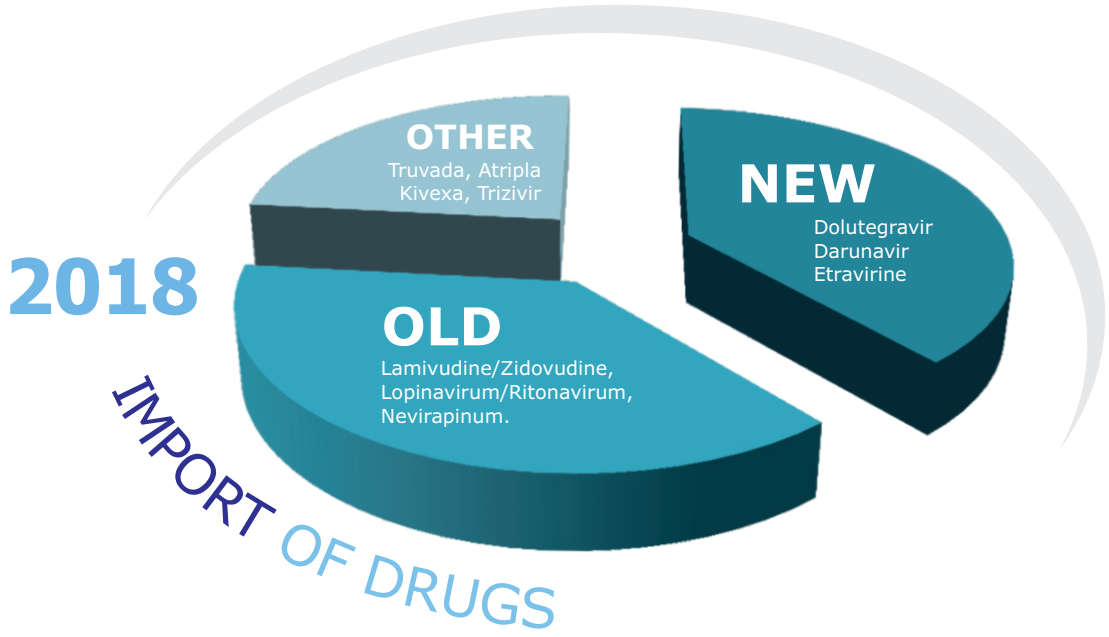
1. Compared to 2017, the regulatory framework has been finalized as it pertains to procurement through international organizations and corresponds to the necessary objectives. The point requiring improvement is the expansion of the range of international organizations that provide drug supply services.

2. In 2018, the procurement of only original products for children was enshrined in law, which does not correspond to general global trends and distinguishes Kazakhstan, as the only country in the world that has deprived HIV-children of access to new forms of medicines developed by generic companies.

3. The HIV treatment protocol for adults requires revision due to 2018 WHO recommendations.

4. The lowest cost-effectiveness is still the procurement of drugs from a domestic supplier, which, despite a 5% price reduction under the contract, exceeds the price of the original significantly.

5. 2018 was the first year when the number of new procured drugs increased by far - Dolutegravirum, Darunavir, and Etravirine. The amount of purchased «old» medicines has also reduced significantly - Lamivudine/Zidovudine, Lopinavirum/Ritonavirum, Nevirapinum.



6. Procurement through UNICEF is still the most cost-effective in terms of reducing prices for medicines.

7. The main treatment regimen in Kazakhstan is Tenofovir/Emtricitabine/Efavirenzum.

Recommendations:

1) To expand the procurement of drugs through international organizations, which will result in lower prices and increased patient coverage. Procurement through UNICEF must begin in the first half of the year so that in the absence of medicines, it is possible to hold a national tender.
2) To consider the use of Atazanavir/Ritonavir registered in Kazakhstan as a second-line treatment in accordance with the WHO protocols.
3) To expand the range of international organizations that provide services for the procurement of ARV drugs, since at the moment procurement is only possible through the organizations established by the United Nations General Assembly.
4) To expand the range of prequalification (FDA) when procuring through international procurement agencies, as only WHO prequalification is currently accepted. This measure will help expanding the circle of ARV medicines suppliers when procurement is made through international agencies.
5) To revise measures to support domestic producers, in order to optimize the cost of ARV therapy, as well as to reduce prices and increase patient coverage. The transition from long-term supply contracts with the inability to influence (reduce) artificially high prices, to support measures in the form of subsidizing factories, with the obligation of domestic producer (DP) to reduce prices.
6) To apply flexibilities of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) to lower prices for the procured drugs.

Research on procurement of VHC drugs

1. The viral hepatitis C treatment protocol for adults contains all current recommendations for diagnostics and treatment available today. It complies with all recommendations of[1], EASL[2], AASLD[3].
2. In 2018, the purchase of medicines for the treatment of viral hepatitis C was increased several thousand times.
3. Procurement of drugs for the treatment of viral hepatitis C through the international UNDP organization[4] proved to be the most cost-effective in terms of reducing prices for the medicines.
4. The main treatment regimen for viral hepatitis C in the Republic of Kazakhstan is Sofosbuvir and Daclatasvir.
5. All patients regardless of the degree and severity of the disease are eligible for free drug supply for the treatment of viral hepatitis C.

Recommendations:

1. To review the treatment protocol for viral hepatitis C in adults due to the new WHO recommendations issued in 2018;
2. To conduct screening of the population for viral hepatitis, as recommended by WHO;
3. to launch the National Registry of Patients with Viral Hepatitis;
4. To expand the list of drugs used in the treatment of viral hepatitis C according to WHO recommendations;
5. To expand the procurement of drugs through international organizations, which will result in lower prices and increased treatment coverage for newly identified patients. In order to further reduce prices and expand access to treatment for medicines, procurement should be made through a bid issue among international organizations. When choosing a supplier, attention should be paid not only to the offered price but also to the terms of delivery and terms of payment under the Contract;
6. To expand the list of international organizations providing drugs procurement services;
7. To expand the list of prequalification in the procurement of drugs through international procurement agencies. When procuring, use more extensive use of TRIPS and other flexible provisions to reduce the price of the purchased drugs.

Analysis of intellectual property barriers to access to generic drugs in Kazakhstan.

The intellectual property (IP) section details the existing standards for the protection of IP in the legislation of the Republic of Kazakhstan. Having accessed the WTO, Kazakhstan specified TRIPS and TRIPS-plus provisions in its legislation. This has contributed to the development of both observation and protection of intellectual property rights in the field of medicines. From the point of view of access to treatment for people with HIV, the issues related to intellectual property are extremely relevant, along with all the special features of the legislation that currently affect the range and pricing of available drugs.

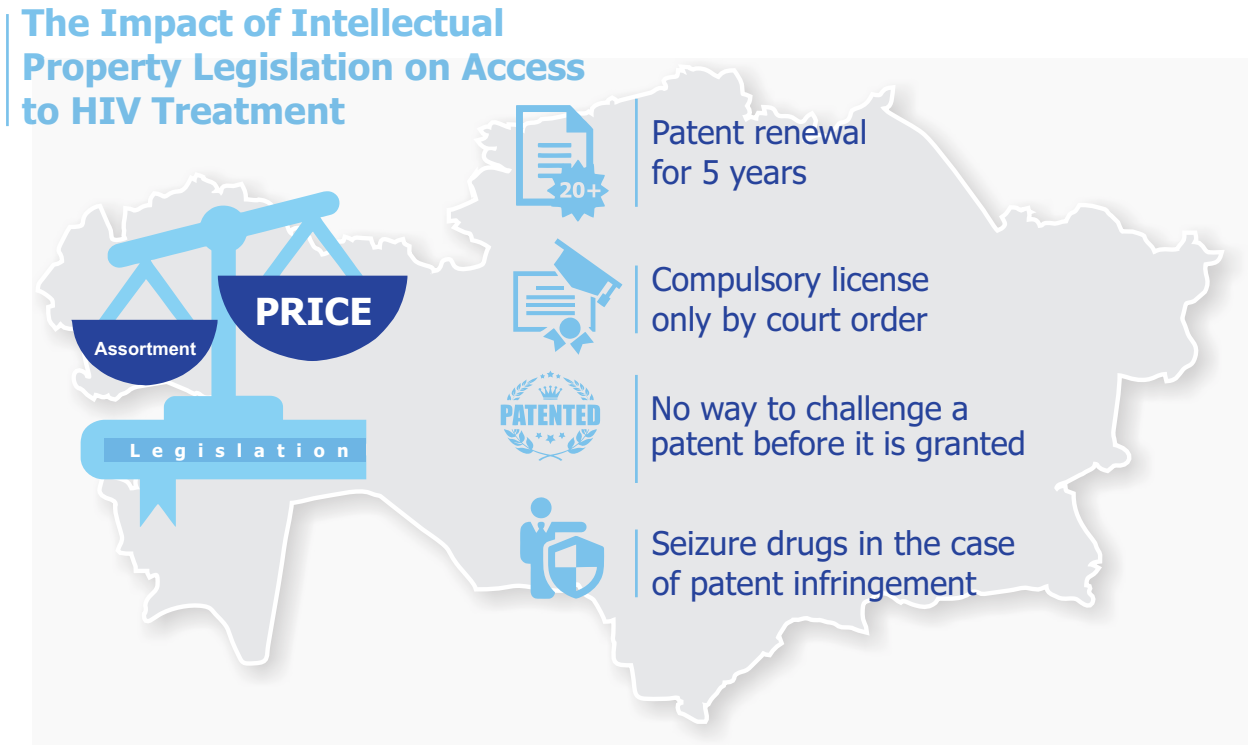
There are statutory regulations of the Republic of Kazakhstan that prevent the emergence of generic drugs, and therefore complicates access to treatment for HIV patients:

These items are as follows:

- The possibility of extending the duration of the patent for an additional 5 years after the established period of validity (20 years) has expired.

- Compulsory License. This item makes it possible to expand the access of a number of patients to the newest HIV drugs, due to a significant reduction in prices. Unfortunately, the legislation of Kazakhstan only considers one of the existing options for issuing such a license - through legal proceedings with a patent holder.

[1]the World Health Organization;
[2]European Association for the Study of the Liver;
[3]American Association for the Study of Liver Diseases;
[4]United Nations Development Programme;



- While in patient-centered countries other options are also provided, such as issuing a compulsory license by the patent office in consultation with the Ministry of Health, with an appropriate statement of reasons.

- Lack of possibility to dispute a patent "before" its issuance, although it is much easier to dispute forthcoming of a patent than to go through all instances of a court to dispute a patent after its issuance.

- Parallel imports in Kazakhstan are provided for under the regional exhaustion mode, that is, if somewhere in the EAU territory the patent holder introduced a drug at a price lower than in Kazakhstan. Our country has the right to purchase this drug in the country where it is cheaper for further use in Kazakhstan.

- "Patent linkage" - In the event that a generic drug enters the market under a valid patent, the right holder has the right to request suspension of the current registration certificate for this medicine, as well as withdrawal of the received batch of goods. This clause does not provide for the interests of patients in terms of the occurrence of treatment interruptions. Since during withdrawal of a batch of drugs, it will be necessary to carry out all the procurement procedures again, which take several months for many ARV drugs.

- "Data Exclusivity" - a ban on dissemination of information on the registration dossier of a new drug for 6 years, this measure blocks the ability of generic companies to develop copies of a new drug. Entering the market for generic versions of a drug directly depends on when generic manufacturers began its development.

RECOMMENDATIONS:

To limit the patent duration to 20 years without the option to renew

To introduce the concept of challenging a patent "before" granting a patent.

To introduce the concept of the "government use" - issuing a compulsory license for drugs on the basis of an order of the National Patent Office and the Ministry of Health, for the benefit of public health.

In the event of the IP rights infringement claim from a patent holder, due to the form supply of generic drugs to ensure the statutory free medical assistance and CSHI, where there is a valid patent, **to abolish the withdrawal of the lot received**.

Recommendations:

1. To limit the patent duration to 20 years without the option to renew.

2. To introduce the concept of challenging a patent "before" granting a patent.

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4. To introduce the concept of the "government use" - issuing a compulsory license for drugs on the basis of an order of the National Patent Office and the Ministry of Health, for the benefit of public health.

5. To apply the international exhaustion regimen for parallel importation procedures.

6. To eliminate the "Data Exclusivity" concept in order to stimulate the competitive environment and reduce the price of medicines, after expiration of the patent.

ANTIRETROVIRAL DRUGS PROCUREMENTS TO ADDRESS HIV/AIDS TREATMENT

INTRODUCTION

The HIV epidemic is maintained at the concentrated stage in Kazakhstan. As of December 31, 2018, the estimated number of people living with HIV has reached 27,000. **19,384** HIV positive persons (71.79 % of the estimated number) were accepted for outpatient treatment.

A total of 35,777 cases of HIV infection were registered as of December 31, 2018, out of which 2,106 cases among foreign citizens, 596 among anonymously surveyed persons and **33,075** cases recorded among citizens of the Republic of Kazakhstan.

The total number of people living with HIV (PLHIV) is **22,712**, the prevalence rate of PLHIV per 100,000 populations is 126.8 (minus those who died of HIV/AIDS, anonymously identified individuals and foreign nationals as of December 31, 2018).

The highest prevalence of PLHIV was registered in the Pavlodar region (244.9), Karaganda region (234.8), Almaty (228.1), East Kazakhstan region (197.9), North Kazakhstan region (190.3), Kostanay region (175.1) and Astana (128.2).

Since 2011, the proportion of affected of sexual transmission has been constantly increased (52% in 2011, 63% in 2016, and 66.7% in 2017).

Since 2011, there has been an increase in sexual transmission in Kazakhstan (2011– 52%; 2016 - 63%; 2017 - 66.7%, and 2018 - 68.4%).

For the last 12-month period of 2018 the share of people infected with drugs injections was **28.3%** (30.2% in 2017); the share of sexual transmissions was **68.4%** (66.7% in 2017), including the heterosexual contact - **63.6%** (61.9% in 2017) and the homosexual contact- **4.8%** (4.8% in 2017); the unspecified causes - **2.4%** (1.8% in 2017), and the vertical transmissions - 0.8% (1.2 in 2017).

Mortality Rate

In 2018, AIDS-related mortality reached a rate of 11.6 per 1000 PLHIV (10.2 per 1000 PLHIV in 2017). Thus, the death rate from AIDS in Kazakhstan is growing.

ARV Therapy

Since 2009, in Kazakhstan the purchase of ARV drugs for adults and children is provided entirely through public funding. Health care services for PLHIV are provided within the national Statutory Free Medical Assistance (SFMA) program.

In line with the World Health Organization (WHO) guidelines, the HIV/AIDS treatment and prevention medical practice guideline documents related to the WHO's 'test and treat' strategy was developed and approved in Kazakhstan in accordance with the recommendations of the WHO 2016[5]. The new treatment guidelines were introduced on January 1, 2018.

In 2018, **4,848** PLHIV were newly diagnosed while **2,699** PLHIV resumed their treatment.

[5]The Clinical protocol No 21 dated May 12, 2017 for the diagnosis and treatment of HIV infection in adults.

Figure 1.1 Proportion of the estimated number of PLHIV and PLHIV with undetectable viral load

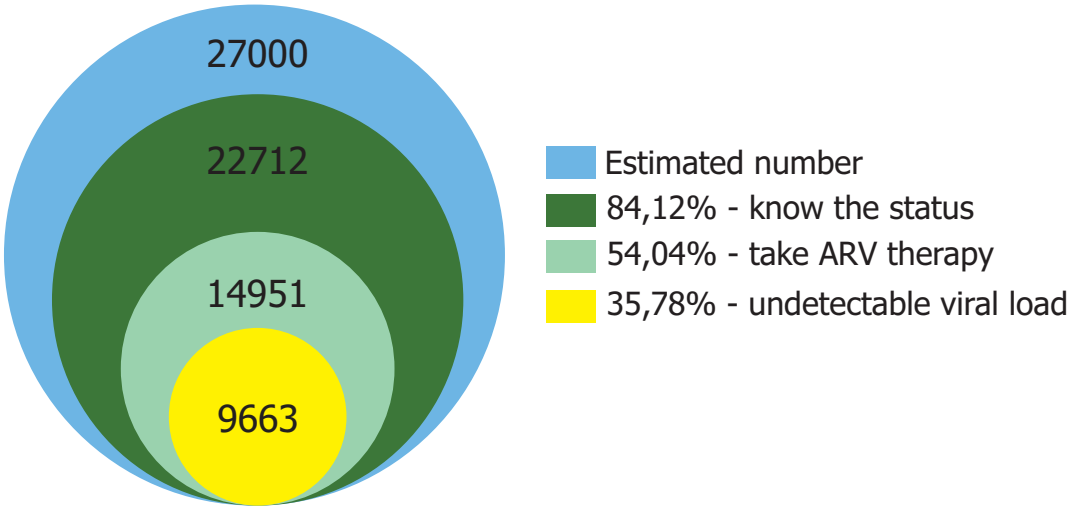
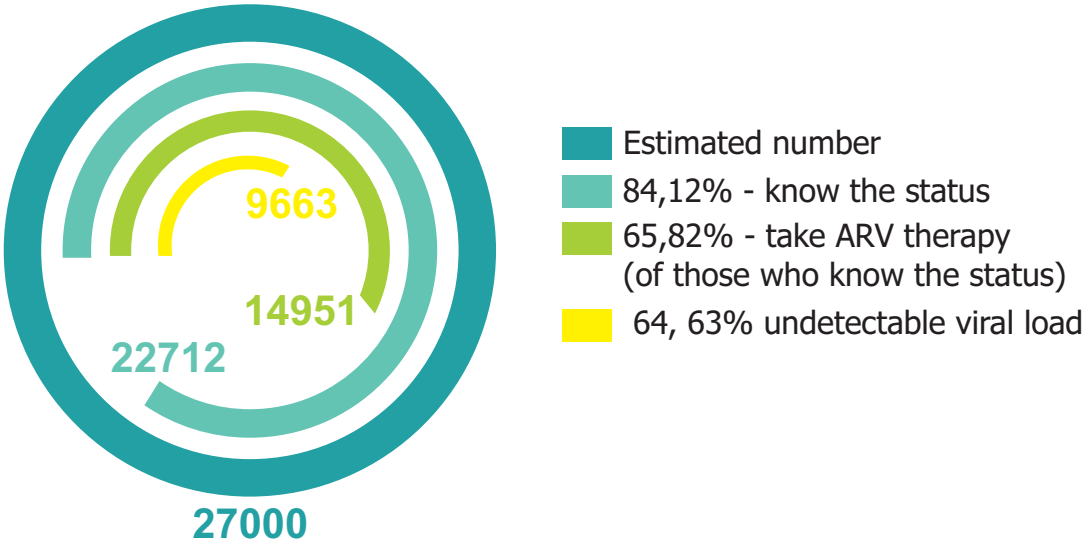


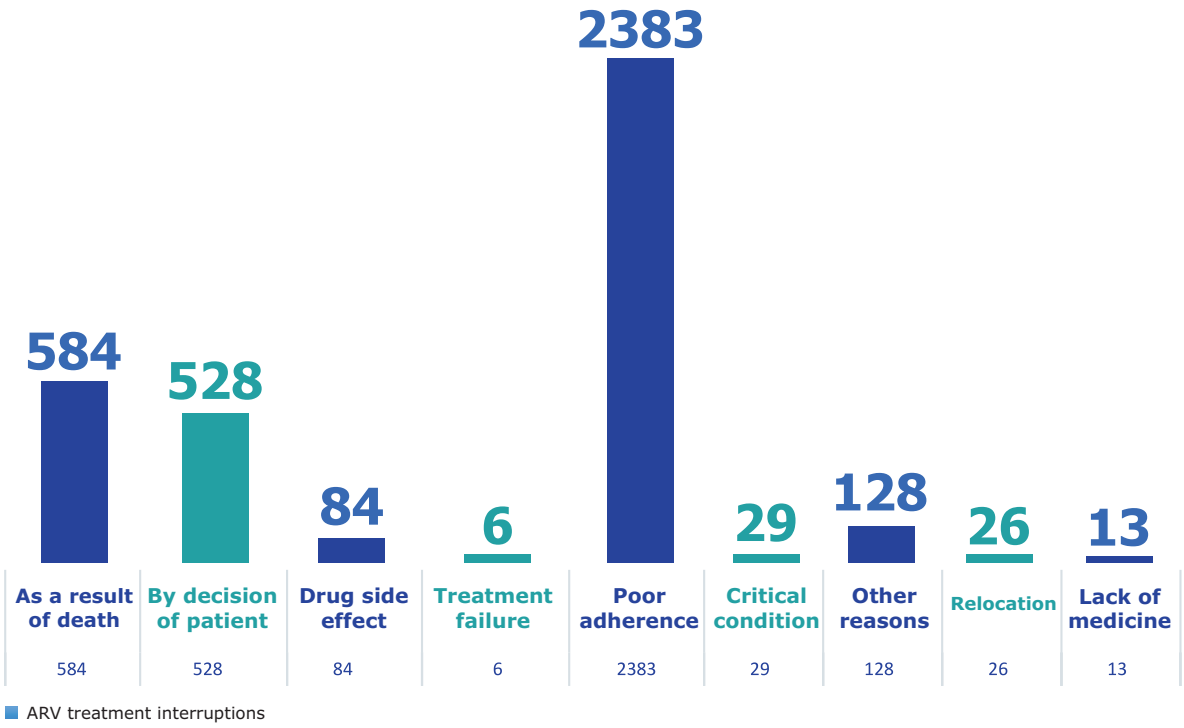
Figure 1.2. Treatment cascade



In 2018, the total number of PLHIV who received ARV therapy within national treatment program was 14,951 (65,82% of those who know the status, or 54.04% of the total estimated number of PLHIV). The number of people with undetectable viral load has reached 9,663 (64.63% of those who take the ARV therapy, or 35.78% of the total estimated number of PLHIV).

However, **3,781** patients interrupted the course of treatment for various reasons, of which 2,383 patients stopped ART due to poor adherence, 84 - due to drug side/toxic effects, 528 PLHIV refused to take therapy, and **584** PLHIV stopped ARVT as a result of death (Figure 2 indicates the reasons for discontinuation of the antiretroviral therapy).

Figure 2. Reasons for the ARV treatment interruption



METHODOLOGY

The purpose of this report is to provide an overview and analysys of key aspects of the public procurements system referring to the antiretroviral drugs and drugs for treating HCV in 2018 and to make appropriate recommendations aimed at improving the drug supply system in the Republic of Kazakhstan.

The data collected were mainly as of the end of December 2018 and provided by the Single Distributor and the Republican Center on Prevention.

The focuses of this report are on the legislation regulating the medications' expertise and drugs registration, the process of budget requests and the procurement process of the antiretroviral drugs.

The information contained in this report has been taken from public sources such as https://medelement.com/, http://www.dari.kz/.

OVERVIEW OF THE REGULATORY FRAMEWORK

Since 1996, HIV/AIDS prevention activities have been implemented in Kazakhstan in line with the following programs:

- National Program on AIDS Response in the Republic of Kazakhstan for 1996 -2000;
- National Program on AIDS Response in the Republic of Kazakhstan for 2001 - 2005;
- National Program on AIDS Response in the Republic of Kazakhstan for 2006 - 2010;
- «Salamatty Kazakhstan» state healthcare development program for 2011-2015;
- «Densaulyk» state healthcare development program for 2016-2019.

In Kazakhstan, health and social care and social services for people living with HIV and AIDS patients are provided in accordance with the Code of the Republic of Kazakhstan « On health of the population and the healthcare system» of September 18, 2009, No. 193-IV.

ARV therapy is prescribed in accordance with the Guidelines for the Clinical Diagnosis and Treatment of HIV Infection in Adults No 21 dated by May 12, 2017.

BUDGET LEGISLATION

In Kazakhstan, medicines for treating HIV are purchased by budgetary funds. The funds direct from the national budget to the Social Health Insurance Fund (SHIF) in the form of transfers[6].

The Ministry of Health in coordination with the Social Health Insurance Fund develops a budget request[7] that includes all necessary calculations such as number of patients, required amount of medicines, etc. Subsequently, by May 15 of the present year, the budget request is to be addressed to the Ministry of Finance, which draws up and submits the national budget for approval by the National Budget Commission. Review of the proposed budget should be completed before August 1 of the current financial year, after which and no later than August 15 it is submitted for consideration to the Government of the Republic of Kazakhstan. The Government shall submit a draft law on the national budget to the Parliament of the Republic of Kazakhstan no later than September 1 of the present year. The adoption of the law on the national budget will take place no later than December 1 of the current financial year. Further, the Government Resolution on National Budget Implementation will be issued within 7 calendar days since the law being signed by the President of the Republic of Kazakhstan. A separate Government Decree sets out the procedure for the use of the transfers.

The amount of funds allocated specifically for the provision of medicines to PLHIV is calculated at the budget proposal stage and is based on data from previous periods. This calculation is carried out by the SHIF. These calculations are not published. In addition, the budget is amended throughout the year, taking into account savings and additional needs. In this regard, it is not possible, at this stage, to provide reliable data of budget allocations for HIV medication disaggregated by year.

DRUGS AUTHORIZATION PROCEDURES

According to the current legislation of the Republic of Kazakhstan, medicinal products (MPs) are subject to state registration.

Drugs produced in the Republic of Kazakhstan, as well as imported to its territory are subject to state registration and re-registration, including:

1) medicinal products with trade names indicating the dosage form, dosage, and type of packing;
2) brand-name drug;
3) bulk products of medicines and health care products;
4) new combinations of medicines previously registered in the Republic of Kazakhstan, indicating the dosage form, dosage, and type of packing;
5) medicines registered earlier in the Republic of Kazakhstan and produced by other manufacturing organizations, in other dosage forms, with a new dosage and type of packing, other composition of excipients and the names;
6) medicinal substances not manufactured in good manufacturing practice;
7) medicines of single marketing authorization holder produced in different countries at different production sites;

It is allowed to import into the Republic of Kazakhstan unregistered drugs on the basis of a conclusion (authorization document) issued by an authorized body if they are intended for procurement by the SD and supplied by international organizations established by the United Nations General Assembly and (or) prequalified by the World Health Organization, except medicines and medical devices under long-term supply contracts.

[6]The Budget Code of the Republic of Kazakhstan №95-IV of December 4, 2008, Art. 35, P.2-2.
[7]Order of the Minister of Finance of the Republic of Kazakhstan dated by November 24, 2014 No. 511 concerning approval of regulations on budget requests.

Drugs (including those not registered) intended for humanitarian aid or emergency assistance are imported into the Republic of Kazakhstan on the basis of a special conclusion (a permit).

An obligatory condition for obtaining state registration, re-registration, or modification of the drug registration dossier is the examination of the medicinal product[8], carried out by the National Centre for Expertise of Medicines, Medical Devices and Medical Equipment.

An obligatory condition for obtaining state registration, re-registration and modification of the drug registration dossier is manufacturing organizations having a **Good Manufacturing Practice (GMP) certificate[9].**

Expert examination of drugs, with the exception of drugs manufactured in the Republic of Kazakhstan or ICH countries[10], shall be carried out within a period not exceeding 210 (two hundred and ten) calendar days.

Expert examination of drugs in obtaining state registration depends on the types of proposed changes and is carried out within a period from 30 to 120 (one hundred twenty) calendar days[11].

Examination of drugs produced in the Republic of Kazakhstan is carried out for 180 (one hundred eighty) calendar days.

Examination of drugs produced in the ICH countries is carried out for 180 (one hundred eighty) calendar days.

After expert examination conducted by the National Centre for Expertise of Medicines, in case of a favorable opinion on safety, efficacy and quality of medicinal products, registration, re-registration or modification of the registration dossier is performed by the Committee of Pharmacy of the Ministry of Healthcare of the Republic of Kazakhstan[12].

[8]Order of the Ministry of Health of the Republic of Kazakhstan dated June 26, 2015 No. 523 "On amendments and additions to the Order of the Ministry of Health and Social Development of RK dated November 18, 2009 No. 735 «On approval of Rules for obtaining marketing authorization, re-registration and modification of the registration dossier of a medicinal product, medical devices and medical equipment».
[9]The countries of the International Conference on Harmonization of Technical Requirements for Registration of drugs for medical use
[10]Order of the Ministry of Health of the Republic of Kazakhstan dated June 15, 2018 № 374 " On amendments to the Order of the Ministry of Health dated November 18, 2009 No. 736 «On approval of the Rules for the examination of medicines, medical devices and medical equipment»
[11]Order of the Ministry of Health of the Republic of Kazakhstan dated April 28, 2015 No. 293 «On approval of standards of public services in pharmaceutical business».
[12]Order of the Ministry of Health and Social Development of RK dated November 18, 2009 No. 735 « On approval of Rules for obtaining marketing authorization, re-registration and modification of the registration dossier of a medicinal product, medical devices and medical equipment».

PROCUREMENT PROCEDURE FOR THE MEDICINAL PRODUCTS, INCLUDING ANTIRETROVIRAL AGENTS AND HCV DRUGS, USING THE NATIONAL BUDGET FUNDS

Procurement of MPs (Medicinal Products), including antiretroviral agents, within the framework of the SFMA (Statutory Free Medical Assistance) and in the CSHI (Compulsory Social Health Insurance) system is excluded from the public procurement legislation of the Republic of Kazakhstan[13]. MP procurement procedures are in compliance with the Governmental Decree of RoK 719[14].

Medicinal Products intended for the provision of the SFMA and additional medical care are purchased under the INN (international non-proprietary names), and in case of individual patient intolerance - under the TN (trade names). In case of procurement of a polycomponent medicinal drug, its composition must be indicated[15].

For optimal spending of funds allocated for the procurement medicines intended for the provision of the SFMA, medicines are purchased at maximum prices not exceeding the limits established by a competent authority. In 2018, the price limits for the list of Sole Distributors have been approved by the Order of the Ministry of Health of the Republic of Kazakhstan No. 631.

In the absence of quoted prices for medicines within the framework of the SFMA, the price ceiling is not determined and no procurement is carried out under the SFMA[16].

Limit prices for TN are regulated by the Order of the Ministry of Health of the Republic of Kazakhstan No. 931[17].

Medical assistance to HIV-infected persons is provided through a Single Distributor.

Sole Distributor (SD) is a legal entity that carries out the purchase of Medicinal Products as part of the SFMA and within the within the CSHI system, enters into agreements, including long-term contracts.

In the Republic of Kazakhstan, the Sole Distributor is SK-Pharmacy LLP, 100% owned by the state.

The SD purchases ARV drugs as follows: through a two-stage tender; from single source; through a special procedure for the procurement of medicines to prevent the occurrence and spread of infectious and parasitic diseases, prevent and eliminate the consequences of emergency situations; through a special procedure under long-term supply contracts from suppliers who intend to establish a manufacture of medicinal drugs or have a production of medicinal products.

Customers (government agencies, Compulsory Medical Insurance Funds, medical organizations executing government order) for procurement under the list of a Sole Distributor submit applications to SD, on the basis of which the SD makes procurement.

[13]Code of the Republic of Kazakhstan «On the Health of the People and the Health System», Art. 2,p.2.
[14]Decree of the Government of the Republic of Kazakhstan dated November 8, 2017 No. 719 "On Amendments to the Governmental Decree of the Republic of Kazakhstan No. 1729 dated October 30, 2009 «On Approval of the Rules for Organization and Conduct of Procurement of Medicines, Preventive (Immunobiological, Diagnostic, Disinfecting) Drugs, Medical Devices and Medical Equipment, and Pharmaceutical Services to Provide statutory free medical assistance and medical care in the compulsory social health insurance system» and dated July 8, 2015 No. 515 «On approval of the Rules for the procurement of services for the storage and transportation of medicines and medical products by a single distributor in the framework of the guaranteed volume of free medical care and the compulsory social health insurance system and the introduction of amendments and additions to some decisions of the Government of the Republic of Kazakhstan».
[15]Code of the Republic of Kazakhstan «On the Health of the People and the Health System», Art. 76
[16]Order of the Ministry of Health of the Republic of Kazakhstan No. 53 of February 8, 2018 "On Amending Order the Acting Minister of Health and Social Development of RK dated July 30, 2015 No. 639 «Pricing Policy for Medicines and Medical Products within the Statutory Free Medical Care»
[17]Order of the Minister of Health of the Republic of Kazakhstan of December 8, 2017 No. 931 "On Approval of the Kazakhstan National Medicinal Formulary"

Two-Stage Tender:

Announcement of a two-stage tender is published on the Internet resource of the Sole Distributor.

When calculating the amount allocated for the purchase, the SD reduces the marginal prices for each lot by the amount of SD's markups.

If procurement is made by a two-stage tender or any of its lots is declared invalid, Sole Distributor makes one of the following decisions:

1) on the repeated procurement by a two-stage tender;
2) on changing conditions of a two-stage tender and the repeated procurement by a two-stage tender;
3) on a single source procurement;
4) on cancellation of procurement in the absence of customer demand.
5) on the implementation of procurement in a special order.

Before the delivery contract is signed, the SD negotiates with the supplier to reduce the price of the supply contract. The SD forms and places a protocol on the results of the purchase on an Internet resource and concludes a supply contract.

One of the procurement principles in purchasing medicines is the support of domestic producers.

The following support measures apply to DP (Domestic Producers):

In case of participation in the DP tender, the tender application of which meets the requirements of the procurement rules, the commission recognizes such a supplier as a winner without applying a single source procurement method.

If more than one supplier participating in the tender, only DPs are allowed to participate in the tender.

In case of participation of the DPs in the tender for lots providing for the signing of a long-term supply contract, the SD enters into a long-term supply contract (up to 10 years) without applying a single source procurement method.

However, DP (Abdi Ibrahim Global Pharm), supplying ARV medicines as part of the SFMA in Kazakhstan, does not assume any obligations to ensure an affordable price, and since February 2018, this company is legally entitled to exceptional opportunities not to comply with the pricing rules for other generics. The only obligation of DP is to reduce the price by 5% annually for 5 years[18].

Kazakhstan supports the entrepreneurial initiatives

The advantage of contracting under the SFMA is available to potential suppliers who have received a certificate of compliance with the following requirements:

- Good Manufacturing Practice (GMP) in the procurement of medicines and signing of long-term contracts for the supply of medicines and medical devices;
- Good Distribution Practice (GDP) in procurement of medicines and pharmaceutical services;
- Good Pharmacy Practice (GPP) in the procurement of pharmaceutical services.

[18]Order of the Ministry of Health of the Republic of Kazakhstan No. 53 of February 8, 2018 "On Amending Order the Acting Minister of Health and Social Development of RK dated July 30, 2015 No. 639 «Pricing Policy for Medicines and Medical Products within the Statutory Free Medical Care».

Single Source Procurements are implemented in the following cases:

1) where a two-stage tender as a whole or on any of its lots is deemed invalid;
2) upon receipt of an additional order from customers towards increase in the amount of drugs, as well as procurement to replenish the minimum level of supply during the same financial year;
3) where the winner of the two-stage tender and (or) a potential supplier, who took second place, did not sign within the agreed deadline and avoided signing a supply contract;
4) upon termination of supply contract due to failure to fulfill or improper fulfillment by supplier of its obligations under any supply contract or a long-term supply contract;
5) when purchasing from international organizations or DP of drugs that do not have analogues in the Republic of Kazakhstan.
6) when purchasing from international organizations established by the General Assembly of the United Nations, by resolution of the authorized body in the field of health care, on the basis of international treaties (agreements) ratified by the RK, as well as international treaties signed for their implementation.

Special aspects of procurement through organizations incorporated by the United Nations General Assembly:

- Procurement is made according to the Single Distributor's list;
- Quotation (prices for medical drugs; additional charges associated with the delivery) must not exceed the marginal prices;
- Medical drugs do not include the following: existence of registration, conformity of labeling, consumer packaging and instructions, existence of a registered price for a trade name;
- Shelf life and transportation conditions in accordance with the submitted quotation;
- An advance payment in the amount specified in the agreement is allowed.
- It is allowed to engage third parties to organize the delivery of goods.
- The following requirements, in accordance with the legislation of the Republic of Kazakhstan, do not apply to suppliers: experience in the market of the Republic of Kazakhstan, solvency; existence of any unfair suppliers in the list or suspension of activities, bankruptcy, legal capacity.

Special procedure for the procurement of medical drugs to prevent the occurrence and spread of infections and infestations, to prevent and eliminate the emergency consequences

This is to be performed in the cases of:
1) prevention of the occurrence and spread of infections and infestations;
2) prevention and elimination of emergency consequences.

Special procedure under long-term supply contracts with suppliers who have the intention to establish production of medical drugs or that have an existing drug production.

Execution of a long-term contract for the supply of medical drugs is impossible where medical drugs are registered with two or more domestic producers at the time of the announcement.

In addition to procurement through a Single Distributor through the targeted transfers from the national budget, ARV drugs can also be purchased through the local budget, in cases where the medical drug is included in the SFMA list but not included in the list of a Single Distributor[19]

[19]Government regulation of the republic of Kazakhstan dated November 8, 2017 no. 719 "on amendments to the government regulation of the republic of Kazakhstan dated October 30, 2009 "1729 "on approval of the guidelines for the organization and procurement of medicinal products, preventive (immunobiological, diagnostic, disinfectant) drugs, medical products and medical equipment, pharmaceutical services for the provision of statutory free medical assistance and compulsory social medical insurance system" and dated July 8, 2015 no. 515 "on approval of the guidelines for the procurement of services for the storage and transportation of medical drugs and medical products by a single distributor within the framework of the statutory free medical assistance and compulsory social health insurance system and making amendments and alterations to some government regulations of the republic of Kazakhstan". Chapter 3. p.19.

RESTRICTIVE LISTS OF MEDICINES IN THE REPUBLIC OF KAZAKHSTAN

In the Republic of Kazakhstan, medical care is provided in the following amounts[20]:

1) basic – statutory free medical assistance (SFMA),
2) additional medical care, including:

- medical assistance in the system of compulsory social health insurance (CSHI)[21]
- medical assistance as part of voluntary medical insurance[22].

To ensure the purchase of ARV drugs under the SFMA it is necessary to ensure the presence of medicines in 4 following lists:

- List of registered prices for drugs[23]
- Kazakhstan's National Medicinal Formulary, Order of the Minister of Health Social Development of the Republic of Kazakhstan No 931[24]
- List of medicinal products within the framework of the SFMA and CSHI, the Order of the Minister of Health of the Republic of Kazakhstan No. 666[25]
- List of medicinal products to be purchased by the SD for 2018 with the indication of price ceilings, the Order of the Minister of Health of the Republic of Kazakhstan No631[26]

Any treatment using medicines not included in the formulary of a healthcare organization is carried out on a fee-paying basis at the expense of patients.

Kazakhstan's National Drug Formulary[27] is a list of medicines with proven clinical efficacy and safety, containing information on medicines and prices, which is an obligatory basis for the development of medicinal formularies of healthcare organizations and the development of drug procurement lists within the framework of SFMA and CSHI[28].

Thus, medicines for pharmaceutical assistance to HIV-infected persons should be included in the List of registered prices for drugs, the Kazakhstan National Drug Formulary (Order No 931), as well as in the list of medicines for free and (or) privileged provision of certain categories of citizens with certain diseases (conditions) for outpatient assistance (Order No 666).

However, not all formulary drugs (order No. 931) were included in the List of the SFMA and CSHI for 2018. Thus, the Order No. 622 only contained 15 antiretroviral drugs: Dolutegravir, Darunavir; Zidovudine; Lamivudine; Abacavir; Tenofovir; Nevirapine; Efavirenz; Etravirine, Zidovudine and Lamivudine; Lamivudine and Abacavir; Tenofovira Disoproxil and Emtricitabine; Zidovudine, Lamivudine and Abacavir; Emtricitabine, Tenofovir Disoproxil and Efavirenz; Lopinavir and Ritonavir. **At the same time there are no new drugs, such as Rilpivirine, Lamivudine, Abacavir, Dolutegravir; Darunavir and Cobicistat.**

In order to be purchased by the SD, a medicinal product must be included in the List of Medicines, Medical Devices and Medical Equipment purchased from the Sole Distributor (the Order of the Minister of Health of the Republic of Kazakhstan No. 631 for the year 2018).

[20]The Code of the Republic of Kazakhstan dated September 18, 2009 No. 193-IV «On People's Health and Health Care System», Article 33-1
[21]The Law of the Republic of Kazakhstan «On Compulsory Social Health Insurance»;
[22]The Law of the Republic of Kazakhstan «On Insurance Activities»
[23]Order of the Ministry of Health of the Republic of Kazakhstan dated November 30, 2017 No. 910 On approval of registered prices for medicines and medical products
[24]Order of the Minister of Health of the Republic of Kazakhstan dated December 8, 2017 No. 931. "On approval of the Kazakhstan National Drug Formulary"
[25]Order of the Minister of Health of the Republic of Kazakhstan No. 105 of March 14, 2018 On Amendments to the Order of the Minister of Health of the Republic of Kazakhstan of August 29, 2017 No. 666 "On Approval of the List of Medicinal Products and Medical Products to Provide Citizens with the Guaranteed Volume of Free Medical Care and the compulsory social health insurance system, including certain categories of citizens with certain diseases (conditions) free of charge and / or preferential drugs and means, medical products and specialized medical products on an outpatient level»
[26]Order of the MOH RoK No. 631 «On approval of pharmaceutical products, medical products within the statutory free medical assistance and in the compulsory social medical insurance system procured from the Sole Distributor for 2018»
[27]Order of the Ministry of Healthcare and Social Development of the Republic of Kazakhstan dated May 22, 2015 No. 369. Rules for the development and approval of the Kazakhstan National Drug Formulary
[28]The Code on People's Health and Health Care System», Article.1, p.1, 61-1

The new drugs - Rilpivirine; Lamivudine, Abacavir, Dolutegravir; Darunavir, Cobicistat-were included in the KNDF (Order No931) and not included in the List of the SD (Order No 631).

ARV-MEDICINES IN KAZAKHSTAN

Regestered Products

As of November 10, 2018, marketing authorizations have been obtained for 26 INN (65TN) in the RoK, without reference to various dosages and drug formulations[29].

In Kazakhstan, only 5 INN of the protease inhibitors are registered: Lopinavir/Ritonavir, Darunavir, Darunavir/Cobicistat, Fosamprenavir, and Atazanavir/Ritonavir. Of these, only two INNs are used for the treatment regimens - Lopinavir/Ritonavir and Darunavir+Ritonavir.

Medicines that are not yet included in the necessary lists for the state procurements, but were registered in 2016 - 2017:

- «Complera» (Emtricitabine/Tenofovir/Rilpivirine), Pateone Inc. Company.
- «Triumeq» (Lamivudine/Abacavir/Dolutegravir), Glaxo Operations Company
- «Rezolsta» (Darunavir/Cobicistat), Janssen-Orto LLC Company.
- «Edurant» (Rilpivirine), Janssen-Cilag Company.
- Atazanavir и Ritonavir, Hetero Labs Limited.

In 2018, only new TNs of already existing drugs and no new INNs were registered.
Annex No1 - Table 1. List of registered ARV medicines in Kazakhstan[30].
Annex No6 - Table 6. List of registered medicines to treat HCV in Kazakhstan[31].

REVIEW OF THE CURRENT EDITION OF NATIONAL HIV TREATMENT GUIDELINES WITH REGARD TO RECOMMENDED REGIMENS; COMPARISON OF RECOMMENDED REGIMENS WITH RECENT WHO RECOMMENDATIONS

The national treatment guidelines[32] are compiled on the basis of the WHO Recommendations for 2016[33]. As can be seen from the regimens presented below, the guidelines almost completely reflect WHO recommendations for 2016 on the first, second and third lines of therapy. The preferred first line medicines are as follows: 3TC (or FTC), TDF or EFV.

According to the latest recommendations of the WHO 2018, the first line of treatment should consist of 2NRTIs and the third drug is Dolutegravir, or Efavirenz. Dolutegravir (DTG) is present in the alternative first-line drug regimen, as well as in the alternative second-line drug regimen and in the main scheme of the third-line drug regimen.

For second-line drugs, WHO recommends the use of 2 NRTIs and Lopinavir / Ritonavir, Atazanavir / Ritonavir or Dolutegravir. The difference in the treatment guidelines is the use of also boosted Darunavir in the second-row scheme. The third drug regimen completely repeats the latest 2018 WHO protocols.

[29]http://www.dari.kz/category/search_prep
[30]The list of registered drugs on 10.11.2018, available at: http://www.dari.kz/category/search_prep, https://drugs.medelement.com
[31]Site of the National Center for Registration of Medicines and Medical Devices of the Ministry of Health http://www.ndda.kz/ and KNDF MF RoK http://www.knf.kz/index.php/kz/
[32]Clinical Guidelines for HIV-infection Diagnostics and Treatment in adults No.21 dated 12.05.2017
[33]Consolidated Guidelines for the use of antiretroviral drugs for the treatment and prevention of HIV infection. Recommendations from a public health perspective. Second Edition, 2016.

Table 1. First-line antiretroviral regimens according to the National HIV Treatment Guideline

	Combination of NRTIs		Third drug
	First drug	Second drug	
Preferred 2 NRTIs + 1 NNRTI	3TC (or FTC)	TDF	EFV
Alternative 2 NRTIs + 1 NNRTI	3TC	AZT	EFV
	3TC	AZT	NVP
	3TC (or FTC)	TDF	DTG
	3TC (or FTC)	TDF	NVP
	3TC (or FTC)	TDF	EFV400
Special conditions	3TC (or FTC)	ABC (or TDF)	DTG LPV/r DRV/r or DRV/k RPV ATV/r

Efavirenz 400 is not registered in Kazakhstan, therefore Efavirenz 200 is used to switch to this dosage.

Table 2. Second-line antiretroviral regimens according to the National HIV Treatment Guideline

Preferred regimens	Alternative regimens
AZT + 3TC + ATV/r	AZT + 3TC + DRV/r
TDF + 3TC (or FTC) + LPV/r	TDF + 3TC (or FTC) + DRV/r
	ABC + 3TC (or FTC) + EFV or NVP ABC + 3TC (or FTC) +LPV/r or DRV/r
	AZT (or ABC, or TDF) + 3TC (or FTC) +DTG или RAL
	AZT (or ABC, or TDF) + 3TC (or FTC) +LPV/r + RAL
	TDF + 3TC (or FTC)+ETV

Third-line antiretroviral regimens according to the National HIV Treatment Guideline

DRV/r + DTG (или RAL) ± 1-2 НИОТ DRV/r + 2НИОТ ± ННИОТ

ANALYSIS OF PURCHASES OF ANTIRETROVIRAL DRUGS IN 2018

According to the approved budget, at the beginning of the year it was planned to allocate **KZT 5,275,445,000 or USD 14,064,102.90.**

The total ARV drugs purchase price was KZT 4,822,879,763.40 or USD 12,857,584.01[34].

APPLIED PROCUREMENT MECHANISMS

In 2018 antiretroviral drugs (hereinafter referred to as ARV drugs) were purchased through a Sole Distributor - SK-Pharmacy LLP.

In 2018, the following procurement mechanisms were applied:

- two-stage tender (national tender);
- procurement under long-term supply contracts (LTSC) with domestic producers (DP);
- procurement from a single source (through UNICEF);
- single source procurement (procurement of drugs that do not have analogues in Kazakhstan in terms of INN and (or) drug's characteristics)

Annex 3 below indicates all types of medications purchased by the SD for the year 2018 as of December 2018.

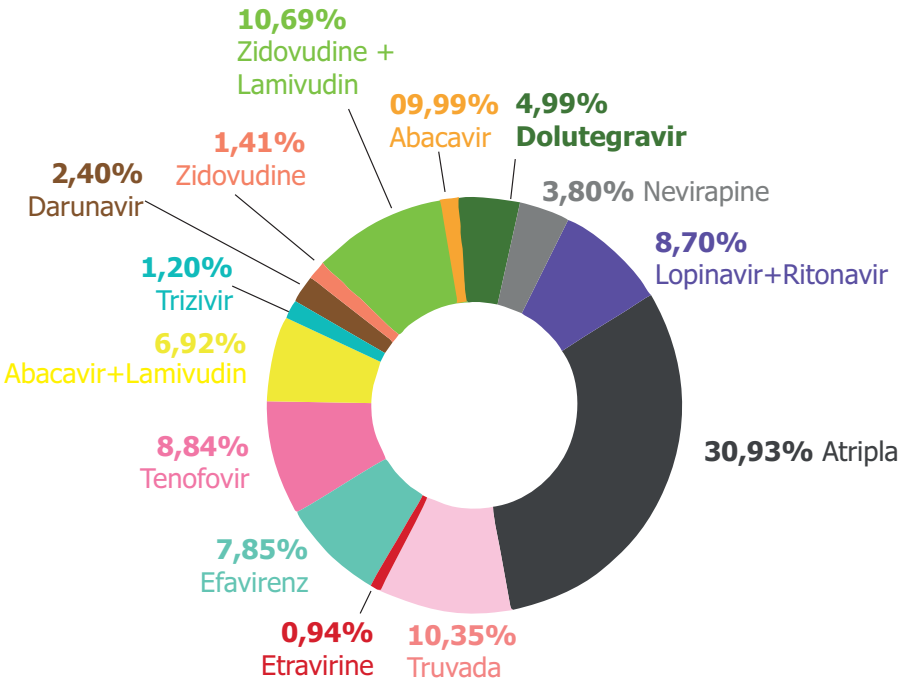
It should be taken into account that the Ministry of Health of the RoK buys only original drugs for the treatment of children[35]. In comparison with previous periods of procurement, in 2018 this norm was first legislated. To this end, the SD conducts bidding procedures to provide for children separately. For the rest of the patients generics are purchased. As a result, both originals and generics with different trade names may be supplied under the same medicine names. Thus, they can be purchased using various procurement mechanisms.

Purchases of ARV Drugs by the Ministry of Health of the Republic of Kazakhstan in 2018

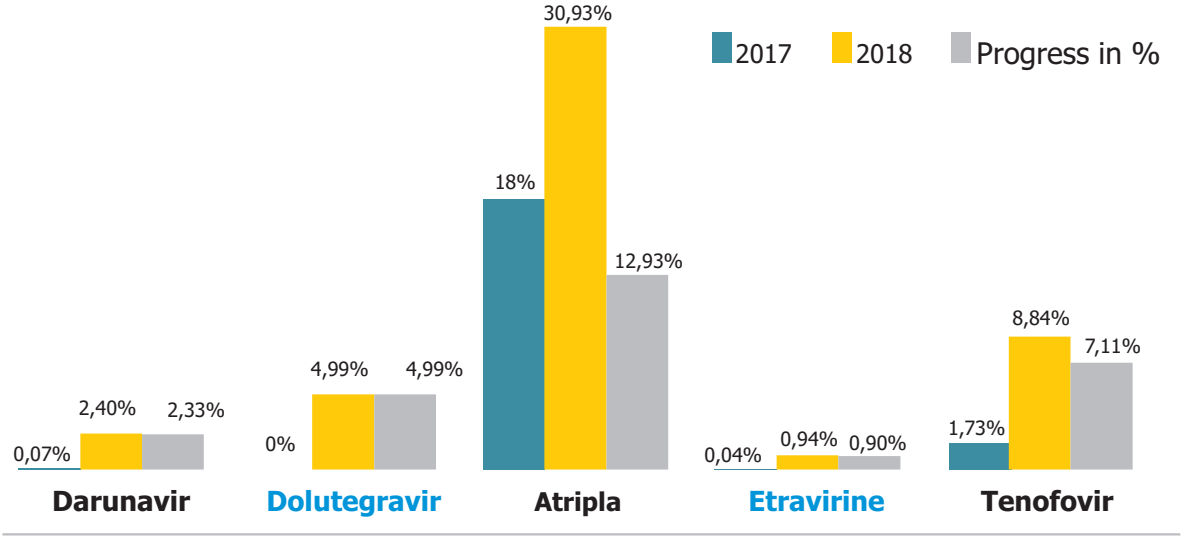
[34]Exchange rate as of January 8, 2019: USD 1 = KZT 375,10

[35]Order of the Minister of Health of the Republic of Kazakhstan No. 105 of March 14, 2018 On Amendments to the Order of the Minister of Health of the Republic of Kazakhstan of August 29, 2017 No. 666 "On Approval of the List of Medicinal Products and Medical Products to Provide Citizens with the Guaranteed Volume of Free Medical Care and the compulsory social health insurance system, including certain categories of citizens with certain diseases (conditions) free of charge and / or preferential drugs and means, medical products and specialized medical products on an outpatient level»

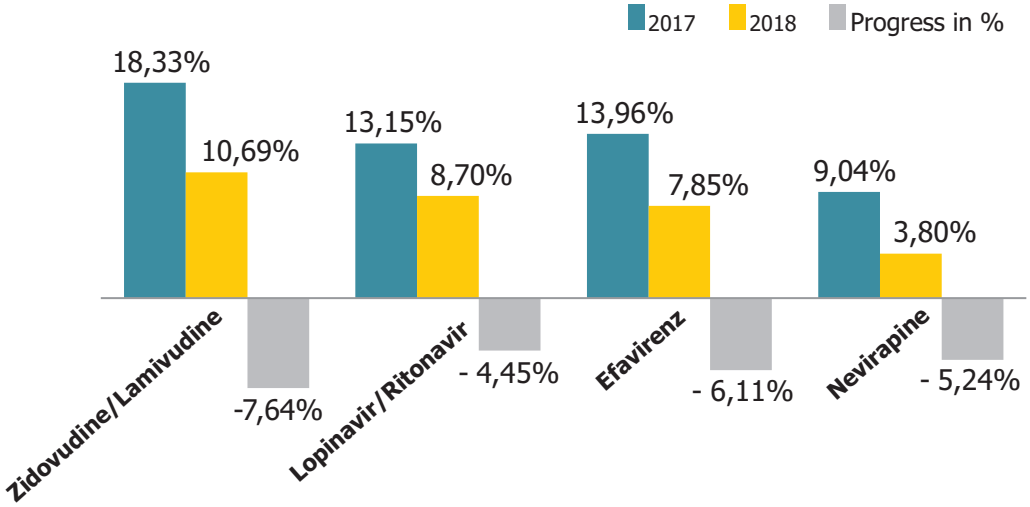
Figure 3. ARV Drugs Purchased by the SD for the year 2018 (by package)



Compared to 2017, in 2018, the purchase of the following drugs was increased (as a percentage of the total purchase of packages): Table 3.



Reduced purchase of drugs (as a percentage of the total purchase of packages): Table 4.



From the total amount of purchased medicines, the following drugs were purchased by a two-stage tender method in the amount of 635.3 million tenge:

Table 5. ARV Drugs Purchased through the two-stage tender method in 2018

INN	Brand Name	Drug dosage form	Manufacturer	Procurement volume	Price of the Supplier, 1 KZT per unit	Price of the supplier, 1 KZT per package	Total Price of the Supplier	Price fall in towards to the allocated amount, %	Dynamics of price changes in 2018 and 2017	Original / Generic
Abacavir, 300 mg	Ziagen®	60	GlaxoSmith Kline Pharmaceuticals Ltd.	23 460,00	466,00	27 960,00	10 932 360,00	▼6,54%	▼14,08%	Original
Abacavir, 300 mg	Ziagen®	60	GlaxoSmith Kline Pharmaceuticals Ltd.	28 560,00	466,00	27 960,00	13 308 960,00	▼6,54%	▼14,08%	Original
Abacavir+ Lamivudine, 300 mg	Kivexa®	30	Glaxo Operations United Kingdom Ltd.	15 240,00	1 240,00	37 200,00	18 897 600,00	▼6,54%	▼3,53%	Original
Abacavir+ Lamivudine, 300 mg	Kivexa®	30	Glaxo Operations United Kingdom Ltd.	27 990,00	1 240,00	37 200,00	34 707 600,00	▼6,54%	▼3,53%	Original
Zidovudine, 100 mg	Retrovir®	100	GlaxoSmith Kline Pharmaceuticals Ltd.	16 400,00	100,60	10 060,00	1 649 840,00	▼6,54%	▼9,94%	Original
Zidovudine, 100 mg	Retrovir®	100	GlaxoSmith Kline Pharmaceuticals Ltd.	35 500,00	100,00	10 000,00	3 550 000,00	▼6,28%	▼10,47%	Original
Zidovudine+ Lamivudine	Combivir	60	GlaxoSmith Kline Pharmaceuticals Ltd.	63 480,00	196,40	11 784,00	12 467 472,00	▼ 6,54%	▼10,73%	Original
Zidovudine+ Lamivudine, 300mg/150 mg	Combivir	60	GlaxoSmith Kline Pharmaceuticals Ltd.	111 060,00	196,40	11 784,00	21 812 184,00	▼1,03%	▼10,73%	Original
Lopinavir + Ritonavir, 200mg/50mg	Aluvia	120	AbbVie Deutschland GmbH & Co. КГ,	654 360,00	173,77	20 852,40	113 708 137,20	▼6,54%	▲2,22%	Original
Lopinavir + Ritonavir, 100mg/25 mg	Aluvia	60	AbbVie Deutschland GmbH & Co,	31 380,00	59,78	3 586,80	1 875 896,40	▼6,54%	▲2,21%	Original
Lopinavir + Ritonavir, 200mg/50mg	Aluvia	120	AbbVie Deutschland GmbH & Co. КГ,	29 760,00	173,77	20 852,40	5 171 395,20	▼6,54%	▲2,22%	Original
Lopinavir + Ritonavir, 100mg/25 mg	Aluvia	60	AbbVie Deutschland GmbH & Co,	84 540,00	59,78	3 586,80	5 053 801,20	▼6,54%	▲2,21%	Original
Lopinavir + Ritonavir, 200mg/50mg	Aluvia	120	AbbVie Deutschland GmbH & Co. КГ,	76 920,00	173,77	20 852,40	13 366 388,40	▼6,54%	▲2,22%	Original
Lopinavir + Ritonavir, 200mg/50mg	Aluvia	120	AbbVie Deutschland GmbH & Co. КГ,	2 022 600,00	173,77	20 852,40	351 467 202,00	▲ 0,78%	▲2,22%	Original

INN	Brand Name	Drug dosage form	Manufacturer	Procurement volume	Price of the Supplier, 1 KZT per unit	Price of the supplier, 1 KZT per package	Total Price of the Supplier	Price fall in towards to the allocated amount, %	Dynamics of price changes in 2018 and 2017	Original / Generic
Lopinavir + Ritonavir, 60 ml	Kaletra®	5	Aesica Queenborough Ltd., Эббви	335,00	3 195,11	15 975,55	1 070 361,85	▼6,54%	▲2,20%	Original
Lopinavir + Ritonavir, 60 ml	Kaletra®	5	Aesica Queenborough Ltd., Эббви	770,00	3 195,11	15 975,55	2 460 234,70	▼6,54%	▲2,20%	Original
Nevirapine, 200 mg	Vira-mune®	60	Boehringer Ingelheim GmbH,	19 200,00	144,00	8 640,00	2 764 800,00	▼6,25%	▲2,13%	Original
Nevirapine, 200 mg	Vira-mune®	60	Boehringer Ingelheim GmbH,	39 960,00	143,00	8 580,00	5 714 280,00	▼5,41%	▲1,42%	Original
Efavirenz, 200 mg	Stokrin®	90	Zhejiang Huahai Pharmaceutical Co., Ltd, China	69 300,00	221,58	19 942,20	15 355 494,00	▼6,54%	▲2,25%	Original

All medicines are originals. These drugs are intended for children (primarily from the South Kazakhstan region, infected in 2006) and are procured as part of a separate tender. As can be seen from the table, the price was reduced in relation to the allocated amount by no more than 7 percent, which is the margin of the SD. Suppliers did not provide further reductions due to lack of competition.

A significant decrease in prices (11.67%) compared to 2017 occurred only for drugs which generic versions are purchased under long-term supply contracts (Zidovudine/Lamivudine, Abacavir and Zidovudine): Table 6.

INN	TN	% of reduction
Zidovudine + Lamivudine	Combivir	▼10,73%
Abacavir, 300 mg	Ziagen	▼14,08%
Zidovudine	Retrovir	▼9,94%

Compared to 2017, the number of drugs purchased from a domestic supplier under long-term supply contracts in 2018 decreased due to the transition to the new treatment guidelines. According to the long-term supply agreements, the costs of drugs in 2018 decreased by no more than 5%. In 2018, KZT 1,334,076,631.6 was spent, which is 35.11% less than in 2017 due to a decrease in the number of purchased packages.

3 drugs for ARV therapy were purchased under long-term supply contracts from the Abdi Ibrahim Global Farm LLP (AIGF): Abacavir, Zidovudine, Zidovudine + Lamivudine. Below is an analysis of the price difference for Original-made drugs purchased in the framework of the tender and drugs supplied under long-term contracts with domestic manufacturers (Table 4.).

The analysis of prices for original products purchased in the framework of the tender and for products supplied by domestic manufacturers under long-term contracts is presented below (Table 4).

Table 7. Price difference between the original and generic ARV drugs of the domestic supplier

№	INN	TN	Packa-gin	Manu-facturer	Procurement volume	Price of the Supplier, per unit	Price of the supplier, per package	Dynamics of price changes in 2018 and 2017	Total amount	Original / generic
1	Abacavir, 300 mg	Virakar	60	AIGF	89 340,00	583,38	35 002,80	-5,00%	52 119 169,20	generic
2	Abacavir, 300 mg	Ziagen	60	GlaxoSmith Kline	52 020,00	466,00	27 960,00	-14,08%	24 241 320,00	Original
3	Zidovudine, 100 mg	Zidoas	100	AIGF	20 800,00	106,15	10 615,00	-5,00%	2 207 920,00	generic

4	Zidovudine, 100 mg	Retrovir	100	GlaxoSmith Kline	51 900,00	100,30	10 030,00	-10,48%	5 199 840,00	Original
5	Zidovudine+ Lamivudine	Duolazide	60	AIGF	1 693 440, 00	755,71	45 342,60	-5,01%	1 279 749542, 40	generic
6	Zidovudine+ Lamivudine	Combivir	60	GlaxoSmith Kline	111 060,00	196,40	11 784,00	-21,44%	21 812 184,00	Original

The analysis demonstrates that the price for three domestic medicines is much higher than that of the originals. The trend of purchasing more expensive products of domestic production continues. It should be noted that the increase in the price of drugs of the domestic manufacturer was not fixed in 2018. In contrast, prices were reduced by 5% under a long-term supply contract, although in 2017, the price for TN Duozide increased by 50%.

Legislation regulating the purchase of generic drugs has been modified February 8, 2018[36]. In accordance with the new order, raising prices for generic drugs before January 1, 2018 is no longer a violation of the law. A long-term supply agreement for ARVs for the period up to January 1, 2018 was concluded only with the Abdi Ibrahim Global Farm.

Most of the ARV drugs were procured through UNICEF in the amount of 1,225,816,694.10 tenge:

Table 8. ARV drugs purchased through UNICEF

INN	Brand Name	Drug dosage form	Manufacturer	Number of units	Allocated amount	Price of the Supplier, 1 KZT per unit	Total Price of the Supplier	Price reduction towards to the allocated amount, %	Dynamics of price changes in 2018 and 2017	Original/ generic
Abacavir+ Lamivudine, 300mg	Kivexa®	30	GlaxoSmithKline Pharmaceuticals Ltd.,	561 780, 00	**518 410 584, 00**	825,29	463 633 219, 51	▼10,50%	Not purchased	Original
Darunavir, 400 mg, 1 tablet Norvira 100 mg with 2 units of the drug (INN – Ritonavir)	Prezista ®	60	Janssen-Orto LLC,	94 740,00	**146 511 619, 20**	1 446,21	137 013 592, 96	▼ 6,48%	▲2,58 %	Original
Darunavir, 600mg, 1 tablet Norvira 100 mg with each unit of the drug (INN – Ritonavir)	Prezista ®	60	Janssen-Orto LLC,	97 140,00	**214 279 530, 00**	2 142,30	208 102 677, 97	▼2,80%	▲ 1,54 %	Original
Darunavir, 800 mg, 1 tablet Norvira 100 mg with each unit of the drug (INN – Ritonavir)	Prezista ®	30	Janssen-Orto LLC,	113 970, 00	**338 040 612, 00**	2 893,09	329 725 970, 19	▼ 2,45%	Not purchased	Original
Zidovudine, 300mg	Zidovudine	60	Micro Labs, India	9 420,00	**269 694,60**	22,42	211 183,62	▼21,69%	▼11,46%	generic
Nevirapine, 200 mg	Nevirapine	60	Mylan Laboratories Limited, India	605 460, 00	**7 145 527,20**	11,04	6 686 498,42	▼ 6,42%	▲ 6,19%	generic
Tenofovir, 300 mg	Tenofovira disoproxila Fumarate	30	Mylan Laboratories Limited, India	772 710, 00	**31 821 307,80**	38,65	29 867 430,84	▼6,14%	▼1,80 %	generic

[36] Order of the Ministry of Health of the Republic of Kazakhstan No. 53 of February 8, 2018 "On Amending Order the Acting Minister of Health and Social Development of RK dated July 30, 2015 No. 639 «Pricing Policy for Medicines and Medical Products within the Statutory Free Medical Care».

INN	Brand Name	Drug dosage form	Manufacturer	Number of units	Allocated amount	Price of the Supplier, 1 KZT per unit	Total Price of the Supplier	Price reduction towards to the allocated amount, %	Dynamics of price changes in 2018 and 2017	Original/ generic
Tenofovir+ Emtricitabine+ Efavirenz, 300 mg/200 mg/600 mg	Tenofovir Disoproxil Fumarate, Emtricitabine and Efavirenz	30	Mylan Laboratories Limited, India	2 703 420, 00	**192 267 740, 70**	69,02	186 597 933, 37	▼2,95%	▼17,08%	generic
Emtricitabine+ Tenofovir, 300 mg/200 mg	Tenofovir Disoproxil Fumarate and Emtricitabine	30	Micro Labs, India	901 440,00	**48 564 538, 50**	43,18	38 924 843,26	▼ 19,85%	Not purchased	generic
Emtricitabine+ Tenofovir	Truvada ®	30	Takeda GmbH , Gilead	2 910,00	**1 981 296,00**	583,55	1 698 122,78	▼14,29%	▲ 1,82 %	Original
Efavirenz, 200mg	Efavirenz	90	Strides Shasun Limited , India,	55 710,00	**2 417 814,00**	34,24	1 907 252,28	▼21,12%	▼1,82 %	generic
Efavirenz, 600 mg	Efavirenz	30	Hetero Labs Limited, India	644 370,00	**17 972 500,80**	26,39	17 007 735,89	▼5,36%	▼21,82%	generic

Thus, 12 types of drugs were procured through UNICEF. Since Kazakhstan purchases drugs through the UNICEF mechanism for more than a year, the percentage of price reduction in 2018 ranged from 2.45% to 21.69% (in 2017, 4.68% to 96.91%).

At the same time, high cost-effectiveness was achieved due to a significant reduction in prices and the resulting expansion of patient coverage with drug therapy. Thus, of all the procurement methods for 2018, procurement through UNICEF provided the greatest price reduction and patient coverage.

From there, a savings of KZT 98,306,303.71 were achieved versus the amount allocated.

Under contracts for the supply of drugs that have no analogues, 6 items were purchased in the amount of KZT 1,432,092,663.76 or USD 3,817,895.66[37].

Table 9.

INN	TN	Drug dosage form	Manufacturer	Number of units	Total allocated amount	Supplier's price, KZT, per unit	Total Price of the Supplier	Price reduction towards to the allocated amount, %
Abacavir, solution 20 mg/ ml, 240 ml	Ziagen®	1	GlaxoSmithKline Inc.,	524,00	12 110 688,00	21 600,00	11 318 400,00	6,54
Abacavir+ Lamivudine+ Zidovudine, 300mg/150mg/300mg	Trizivir®	60	GlaxoSmithKline Pharmaceuticals Ltd.,	209 160, 00	270 517 086, 00	1 208,74	252 820 058,40	6,54
Dolutegravir, 50 mg	Tivicay®	30	Glaxo Operations, United Kingdom Limited	404 250, 00	893 238 885, 00	2 065,07	834 803 201,35	6,54
Dolutegravir, 50 mg	Tivicay®	30	Glaxo Operations, United Kingdom Limited	31 980,00	70 663 647,60	2 065,07	66 040 832, 11	6,54
Zidovudine, 10 mg/ ml, 200 ml	Retrovir®	1	GlaxoSmithKline Inc.,	3 225,00	23 802 177,00	6 897,69	22 245 050, 25	6,54
Etravirine, 100 mg	Intelens®	120	Janssen-Cilag Inc.,	124 080,00	98 947 544,40	747,45	92 743 788,19	6,27
Etravirine, 200 mg	Intelens®	60	Janssen-Cilag Inc.,	95 460,00	152 692 088, 40	1 494,90	142 703 444,30	6,54
Etravirine, 200 mg	Intelens®	60	Janssen-Cilag Inc.,	6 300,00	10 077 102,00	1 494,90	9 417 889,16	6,54

[37]Exchange rate as of January 8, 2019: USD 1 = KZT 375.10

The table demonstrates the the price reduction in relation to the allocated amount was no more than 7%, which is equal to the amount of SD's mark-up.

Considering the fact that drugs for children and adults are purchased separately (for children it is necessarily original drugs), the medicines under the same INN and with the same dosage in the RoK should be treated as different drugs. Accordingly, it is inappropriate analyze their minimum, maximum and average prices, except for the cases when the same original drug is purchased both for children and adults.

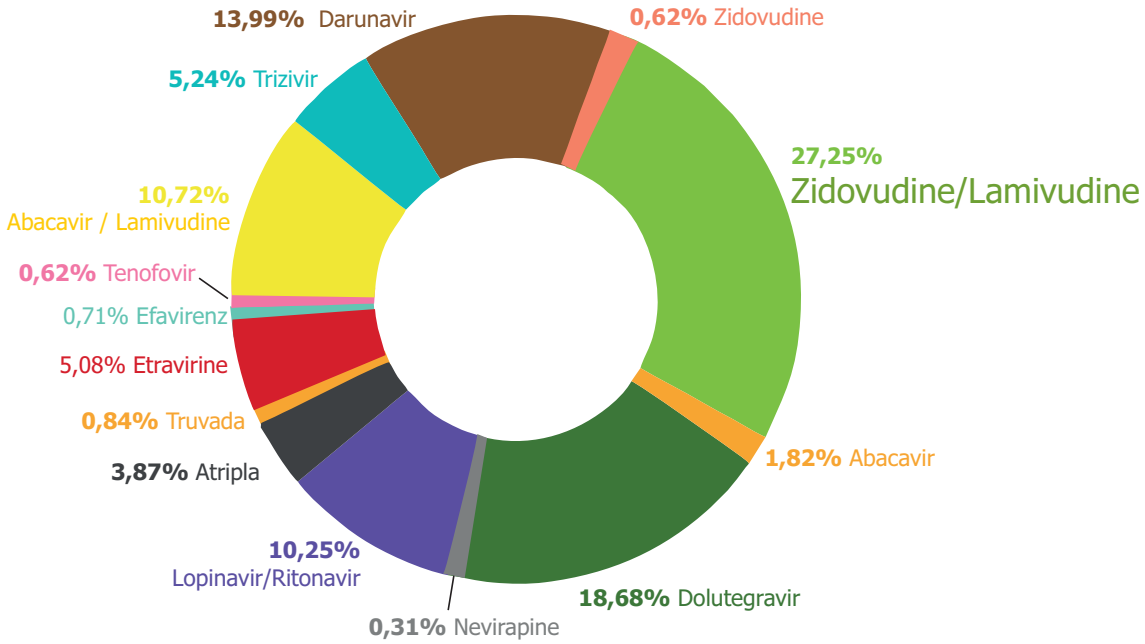
In 2018, only 3 drugs were purchased additionally, and the price of supply differed. Weighted average price was calculated using the following formula: (Price 1 + Price 2 + Price 3) / number of purchases.

Table 10.

INN	TN	Drug dosage form	Manufacturer	Number of units	Minimum supplier price, tenge, per unit	Maximum supplier price, tenge, per unit	Weighted average price of the supplier	Total amount at the price of the supplier	Procurement method
Zidovudine, 100 mg	Retrovir	100	GlaxoSmithKline Pharmaceuticals Ltd.,	51900,00	100,00	100,60	100,30	5 199 840,00	Tender
Nevirapine, 200 mg	Viramune	60	Boehringer Ingelheim GmbH,	59 160,00	143,00	144,00	143,50	8 479 080,00	Tender
Abacavir+ Lamivudine, 300 mg	Kivexa	30	Glaxo Operations United Kingdom Ltd.	605 010,00	825,29	1 240,00	1 101,76	517 238 419,51	Tender, UNICEF

Annex 3 provides the costs of each drug in absolute numbers and as a percentage in the total budget.

Figure 4. Expenditures for ARV drugs as a percentage of the total budget in 2018



Thus, in comparison with 2017, the expenditures for the following medications have decreased due to a decrease in the number of patients:

- Zidovudine/Lamivudine – 27.25 % (48.82% in 2017)
- Trizivir – 5.24% (9.68% in 2017)
- Lopinavir/Ritonavir – 10.25% (14.74% in 2017)

The expenditures for the following medications have increased due to an increase in the number of patients:

- Darunavir – 13.99% (0.42% in 2017)
- Dolutegravir – 18.68% (0% in 2017)
- Etravirine – 5.08% (0.22% in 2017)

The expenditures for Abacavir / Lamivudine (10.72%) also increased due to purchasing only the original version of the drug, due to patent disputes between the originator and the generic. In 2017, a generic version of the drug was purchased (5.64%).

The cost of Truvada (0.84%) decreased due to the purchase of a generic version in 2018 (in 2017, Truvada got 11.34% of the budget due to the purchase of the original version).

Table 2 provides summary data for patient categories: Estimated number of annual courses of treatment of individual ARV drugs, Annex No.5.

Procurement monitoring showed that the main drugs and regimens used for treatment are: TDF+FTC+EFV, TDF+FTC, AZT+3TC, TDF, LPV/r, EFV, ABC+3TC, DTG.

The most common treatment regimens in Kazakhstan are the following[38]: TDF/FTC/EFV, AZT/3TC+EFV, AZT/3TC+LPV/r, AZT/3TC+NVP, TDF/FTC+LPV/r, TDF/FTC+DTG, TDF/FTC+DRV/r. Cases of non-compliance with national treatment protocols are available, but it is clear that they are due to individual intolerance and resistance to certain drugs.

[38]Information on the anti-retroviral therapy regimen used in the period of 01.01.2018 - 31.12.2018 in Kazakhstan. Data providedfor all categories of patients, including children. Republican Center for the Prevention and Control of AIDS.

Table 11. Treatment regimens in Kazakhstan

№	Treatment Regimens	Number of Patients
1	ABC/3TC+EFV (ABC+3TC+EFV)	439
2	ABC/3TC+LPV/r	352
3	ABC/3TC+NVP (ABC+3TC+NVP)	139
4	ABC/3TC+TDF	26
5	AZT/3TC/ABC, (AZT/3TC+ABC), (AZT+3TC+ABC)	269
6	AZT/3TC+EFV (AZT+3TC+EFV)	827
7	AZT/3TC+LPV/r (AZT+3TC+LPV/r)	893
8	AZT/3TC+NVP (AZT+3TC+NVP)	717
9	AZT/3TC+TDF (AZT+3TC+TDF)	17
10	TDF/FTC+EFV (TDF+FTC+EFV)	**7233**
11	TDF/FTC+LPV/r	787
12	TDF/FTC+NVP	362
13	ABC/3TC+DTG	428
14	ABC+TDF+LPV/r	5
15	TDF/FTC+ABC	17
16	ABC/3TC+DRV/r	222
17	TDF/FTC+DTG	880
18	TDF+AZT+LPV/r	2
19	TDF/FTC+DRV/r	559
20	Other regimens	768
Total:		14951[39]

Costs of the first and second lines drugs

The following drugs are included in the preferred and alternative first-line regimens: Lamivudine, Zidovudine + Lamivudine, Efavirenz, Zidovudine, Nevirapine, Tenofovir+ Emtricitabine.

Table 12. Comparison of prices for original and generic drugs of the first-line regimens

Name	Originator, price, KZT	DP (AIGP), price, KZT	Generic, price, KZT.
Zidovudine + Lamivudine	196,4	755,71	Not purchased
Tenofovir+ Emtricitabine	583,55		43,18
Efavirenz, 600 mg	Not purchased		26,39
Nevirapine, 200mg	143,50[40]		11,04
Dolutegravir	2065,07		Not purchased
Tenofovir+ Emtricitabine+Efavirenz	Not purchased		69,02

Since medicines for children are purchased only in the original version, the cost is presented separately for generic and original drugs.

As can be seen from the table, the purchase of drugs from the domestic manufacturer leads to a reduction in the budget allocated for the newer drug groups for people living with HIV.

[39]Procurement data and data of the regimens used may not coincide, since the procurement data as of August 31, 2017 were used for the purpose of this report.
[40]Weighted average price for 2018

Table 13. Cost of the most frequently assigned first-line regimens

Figure	Generic, price, tenge	Original, price, tenge
AZT/3TC+EFV	782,10	222,79[41]
AZT/3TC+NVP	766,75	339,90
TDF/FTC+EFV	69,57	609,94[42]
TDF/FTC/EFV	69,02	Not purchased
TDF/FTC+DTG	2648,62	2108,25[43]

Table 14. Cost of annual courses of the first-line regimens

Figure	Price, KZT		Price, USD	
	Generic	Original	Generic	Original
AZT/3TC+EFV	561302,24	153005,94[44]	1496,40	409,90
AZT/3TC+NVP	559730,18	248069,60[45]	1492,21	661,33
TDF/FTC+DTG	769510,30 [46]	966744,11	2051,48	2577,29
TDF/FTC+EFV	25394,91	222628,72[47]	67,70	593,51
TDF/FTC/EFV	25193,36	Not purchased	67,16	Not purchased

Thus, purchases of first-line drugs from a domestic supplier actually take place at prices of the second line that is 700-1000 USD higher than the cost based on the price of the original drugs.

The following drugs are included in the preferred and alternative second-line regimens: Tenofovir+Emtricitabine, Zidovudine+Lamivudine, Lopinavir/Ritonavir, Darunavir/Ritonavir, Abacavir, Abacavir+Lamivudine, Efavirenz, Nevirapine, Etravirine.

Table 15. Comparison of prices for original and generic drugs of the second-line regimens

Name	Originator, price, KZT	DS (AIGP), price, KZT	Generic, price, KZT
Tenofovir+ Emtricitabine	583,55		43,18
Zidovudine + Lamivudine	196,4	755,71	
Efavirenz, 600 mg	Not purchased		26,39
Nevirapine, 200mg	143,50[48]		11,04
Lopinavir/ Ritonavir, 200 mg/50 mg	173,77		No Generics
Darunavir, 600 mg	2142,30		Not purchased
Abacavir	466,00	583,38	
Abacavir+ Lamivudine	1101,76[49]		Not purchased
Etravirine, 200 mg	1494,90		Not purchased
Dolutegravir	2065,07		Not purchased

Abacavir refers to second-line regimens and is also purchased from a domestic supplier under long-term supply contracts. The price of the domestic supplier for Abacavir exceeds the price of the original drug by 25.10 %.

[41]Using generic Efavirenza since the original EFV was not purchased in 2018.
[42]Using generic Efavirenza since the original EFV was not purchased in 2018.
[43]Using original Dolutegravira since Kazakhstan is under a DTG patent.
[44]Using generic Efavirenza since the original EFV was not purchased in 2018
[45]Weighted average price between supplies
[46]Using original DTG since Kazakhstan is under a DTG patent.
[47]Using generic Efavirenza since the original EFV was not purchased in 2018
[48]Weighted average price for 2018
[49]Weighted average price between supplies

Table 16. Costs of the second-line regimens with a breakdown by generics and original drugs

Figure	Generic, price, KZT	Original, price, KZT
ABC /3TC+EFV		1128,15[50]
ABC /3TC+NVP	1112,80	1245,26
TDF/FTC+ DRV/r	2185,48[51]	2725,85
AZT/3TC +DTG	2820,78[52]	2261,47
ABC/3TC+ DTG	Not purchased	3166,83
TDF/FTC+ETR	1538,08[53]	2078,45

Table 17. Cost of the most frequently assigned second-line regimens

Figure	Generic, price, KZT	Original, price, KZT
AZT/3TC+LPV/r	929,48[54]	370,17
TDF/FTC+LPV/r	216,95	757,32
TDF/FTC+DRV/r	2185,48[55]	2725,85

Zidovudine / Lamivudine is also used in preferred and alternative second-line schemes, and therefore the inefficiency of procurement from the domestic producers also affects the pricing of second-line treatment, thereby increasing the cost of purchasing schemes with Zidovudine/ Lamivudine by 60.18%

Table 18. Cost of annual courses of the second-line regimens

Figure	Price, KZT		Price, USD	
	Generic	Original	generic	Original
AZT/3TC+LPV/r	805372,50[56]	397076,20	2147,08	1058,58
TDF/FTC+LPV/r	269465,17	466698,98	718,38	1244,19
TDF/FTC+DRV/r	1579637,38	1776871,19	4211,24	4737,05

A feature of commonly prescribed second-line regimens is the use of protease inhibitors.

Given the trend to increase the number of patients on Darunavir, the cost reduction of the scheme with Darunavir is possible when using amorphous Darunavir which is not protected by a patent, while ensuring competition between several suppliers of this generic drug.

Lopinavir / Ritonavir purchased for 2018 is more expensive than in 2017 by an average of 2%. Considering the existing patent for the heat-resistant form of Ritonavir and the high share of the budget (10.25%) spent on this drug, the use of TRIPS flexible provisions is necessary to reduce the price.

[50]In 2018, the ABC/3TC was purchased only as original drugs, EFV – only generics
[51]Using original EFV since the generic EFV was not purchased in 2018.
[52]C Using original DTG since Kazakhstan is under a DTG patent protection.
[53]Using original ETR since Kazakhstan is under a ETR patent protection
[54]Using original LPV/r since Kazakhstan is under a LPV/r patent protection
[55]Using original DRV/r since the generic DRV/r was not purchased in 2018
[56]Using original LPV/r, since Kazakhstan is under a LPV/r patent protection

COMPETITION IN THE COURSE OF BIDDING

There is basically no competition for any of the drugs in the drugs procurement procedures for ARV therapy in Kazakhstan.

This is, first of all, due to the following factors:
1) Support of domestic manufacturers under long-term supply contracts;
2) The need to purchase original drugs for children with HIV.

There is no competitive activity when purchasing medicines from domestic manufacturers (3 drugs) under the long-term supply contracts. The supply is made directly, without any tender procedures, at the maximum price allocated for the procurement.

Also, bidding was conducted when procuring 16 drugs for children. However, taking into account social commitment of the state to provide children with original products only, there was virtually no competitive environment during the competitive procedures. Prices were reduced for 3 drugs only. Given that there is no competition in children's tenders, price drops for GlaxoSmithKline medicines is probably due to the fact that the manufacture is dumping in attempt to switch to their drugs adult patients who are currently being provided with home-produced drugs.

Table 4 "Actual prices and contract amounts for ARV drugs purchased in 2018" in Annex 4 below provides detailed breakdowns for prices for each drug per year.

Based on the table, the most expensive drugs were Darunavir / Ritonavir 600 mg (1,563,876.41 tenge), Dolutegravir (753,749.33 tenge) and Etravirine (1,091,279.22 tenge) due to their recent market entry and current patent validity.

The cheapest drugs were generic versions of Tenofovir / Emtricitabine / Efavirenz (25,193.36 tenge) and Tenofovir / Emtricitabine (15,760.97 tenge), as well as generic versions of Efavirenz (9633.94 tenge), Zidovudinea (16365.61 tenge), Nevirapine (8061.88 tenge). This is due to the lack of patent protection for these drugs, as well as procurement through UNICEF.

INTERRUPTIONS

The website pereboi.kz provides an opportunity for feedback. This site is designed to collect information on the absence and interruptions of life-saving drugs for the treatment of infectious diseases, HIV, hepatitis C and tuberculosis by community forces.

A patient may leave information about the following:

- a drug for the treatment of HIV, tuberculosis or hepatitis C was not provided;
- treatment regimen was suddenly changed;
- drugs given for a shorter period than usual;
- gave out syrup instead of tablets or vice versa;
- gave a tablet that needs to be crushed or divided into particles;
- tests for CD4 and viral load was not provided.

In case of a request, the information posted on the website is received by the website consultant. The consultant is a representative of the patient community and is not a worker of a health care institution. The consultant provides information on interruptions to the authorized representative of the Ministry of Health.

12 complaints were received on pereboi.kz/ site in 2018, including the following:
- the inability to pass the test for HIV viral load - 2 messages (Kostanay, Astana),
- replacement of the treatment schemes - 4 messages (Temirtau, Almaty)
- lack of drugs - 3 times (Kokshetau, East Kazakhstan)
- replacement of the form of the drug - 1 treatment (Almaty region)

KEY FINDINGS

The total amount spent on ARV drugs in 2018 was KZT 4,822,879,763.40.

According to the recent WHO recommendations, therapy should be started from the moment of diagnosis, while in Kazakhstan the registered number of PLHIV was 29,384 (71.79% of the estimated number)[57], receiving therapy at the end of 2018 was 14 951 PLHIV (77.13% of those registered or 55.37% of the estimated number of PLHIV). People with an undetectable viral load were 9663 (64.63% of those receiving therapy, or 35.78% of the estimated number of PLHIV).

The main treatment regimens correspond to the WHO recommendations for the first and second line of drugs.

According to WHO recommendations, over the course of procurement process in 2018:

- the purchase of combination drugs Atripla increased up to 30.93% (18% in 2017), Dolutegravir 4.99% (0% in 2017), and Darunavir -2.40% (0.07 % in 2017).
- the number of patients taken Zidovudine / Lamivudine decreased up to 10.69% (18.33% in 2017), Lopinavir / Ritonavir - 8.70% (13.15% in 2017)
- the number of patients taking drugs that are not included in treatment protocols decreased: Abacavir / Lamivudine / Zidovudine 1.20% (2.27% in 2017).

Newer drugs like Rilpivirine; Lamivudine / Abacavir / Dolutegravir; Darunavir / Cobicistat were not purchased, as they were not included in the list of SD (order No. 631) and the list of drugs provided in the frame of SFMA and CSHI (order No. 666).

[57]The data is presented by the Republican Center for the Prevention and Control of AIDS on December 31, 2017

DRUGS TAKING UP THE LARGEST SHARE IN THE BUDGET

- **Zidovudine** (AZT) + Lamivudine (3TC), under the trade name of «Dualazid» – 26.53%. The supplier is a domestic supplier Abdi Ibrahim Global Farm (AIGF). The high inefficiency of the money spent is explained by the price of the drug. The only obligation of this supplier is the annual price reduction by 5%, for 5 years, which they have fulfilled, by reducing the price from KZT 795.49 in 2017 to 755.71 in 2018. However, the cost of the original medicine is equal to KZT 196.40 per unit of Combivir (GlaxoSmithKline).

  The legislation regulating the procurement of generic drugs was amended[58] on February 8, 2018, according to which the formation of overpriced prices for generic drugs before January 1, 2018 is no longer deemed a violation. The long-term supply agreement (until January 1, 2018) for ARV drugs was only signed with Abdi Ibrahim Global Pharma.

18,6%

Dolutegravir (DTG), under the trade name of «Tivikay» – 18.68%. The supplier is the GlaxoSmithKline. The territory of the Republic of Kazakhstan has patent protection for this drug, which adversely affects the price. Dolutegravir is the only integrase inhibitor purchased for 2018.

13,9%

Darunavir (DRV), under the trade name of "Prezista» – 13.99%, the manufacturer - Janssen-Ortholes, the medical drug was purchased through UNICEF. On the territory of the Republic of Kazakhstan, patent protection for this last generation protease inhibitor is applied.

- **Lopinavir (LPV) + Ritonavir (RTV)**, under the trade name of «Aluvia» – 10.25%. The supplier is Ebbwie Deutschland Gmbh. The price was overpriced by 2.21% compared with 2017. The generics of this drug are not registered in Kazakhstan, which has a negative effect on pricing.

- **Abacavir (ABC) + Lamivudine (ZTS)**, under the trade name of Qivexa – 10.72%. The supplier is GlaxoSmithKline. The purchase took place through UNICEF. The budget share was increased both by increasing the number of patients in this scheme in 2018 – 6.92% (5,05% in the procurement for 2017), and due to the purchase of the original drug, due to patent disputes between Aurobindo and GlaxoSmithKline.

[58]Order of the Ministry of Health of the Republic of Kazakhstan No. 53 of February 8, 2018 "On Amending Order the Acting Minister of Health and Social Development of RK dated July 30, 2015 No. 639 «Pricing Policy for Medicines and Medical Products within the Statutory Free Medical Care».

EXISTING OPPORTUNITIES TO SWITCH TO THE NEW ARV MEDICINES

According to the latest WHO recommendations it is recommended to increase the number of people taking Dolutegravir and boosted Darunavir.

Dolutegravir (DTG) is included in the alternative first-line regimens, as well as in alternative second-line regimens and in the main regimen of the third-line of drugs. In 2018, DTG was was purchased for 1,195 treatment courses. Given the increase in the number of patients taking this drug, it can be assumed that in the next edition of the national treatment protocols, Dolutegravir will be presented in a preferred first-line regimen.

Darunavir (DRV/r) is also introduced by the new guidelines as the alternative second- and third-line regimens. In 2018, Darunavir was purchased for 575 one-year treatment courses at the expense of the national budget.

According to the recommendations of the WHO, it is recommended to consider the possibility of further reduction of treatment courses containing Lamivudine / Zidovudine, Nevirapine, Lopinavir / Ritonavir. It is recommended to expand the use of Dolutegravir, Darunavir, Rilpivirine, combination drugs through negotiating a reduction in the prices of original drugs; procurement under direct supplies of certain medicines having no analogues; purchase of new combined, easy to use generic drugs for children; negotiations with the Medical Patent Pool and introducing TRIPS.

FURTHER STEPS REQUIRED TO OPTIMIZE THE PROCESS OF ARV PROCUREMENTS

1) To expand the procurement through international organizations; this will result in lower prices and increased patient coverage. Analysis of procurement mechanisms has shown that procurement through international organizations is the most cost-effective way, resulting in a significant reduction in prices. In this regard, it is necessary to expand procurement, including that of original drugs, through UNICEF. In order for this to happen, procurement through UNICEF must begin in the first half of the year, so that in the absence of drugs (originals), it is possible to hold a national tender.

2) To consider the use of Atazanavir/Ritonavir registered in Kazakhstan as a second-line treatment in accordance with the WHO protocols.

3) To expand the range of international organizations that provide services for the procurement of ARV drugs, since at the moment the system prescribes procurements only through organizations established by the United Nations General Assembly.

4) To expand the range of prequalifications (FDA) when purchasing through international procurement agencies, as currently only WHO prequalification is accepted. This measure will help expanding the number of suppliers of ARV drugs when purchasing through UNICEF.

5) To revise measures to support domestic producers, in order to optimize the cost of ARV therapy, as well as to reduce prices and increase patient coverage. The transition from long-term supply contracts with the inability to influence (reduce) artificially high prices, to support measures in the form of subsidizing factories, with the obligation of domestic producer (DP) to reduce prices

6) To apply flexibilities of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) to lower prices for the procured drugs.

DRUGS PROCUREMENTS TO ADDRESS VIRAL HEPATITIS C TREATMENT

INTRODUCTION

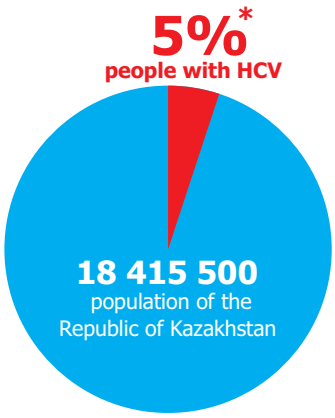
At the present time, the official statistics of the Republic of Kazakhstan has no record on the viral hepatitis incidences across the population, while there are some data regarding the particular target groups.

At the national level, the system of monitoring and evaluation of the preventive medical checkup coverage for viral hepatitis does not exist. By the time the text of this Report was being developed, a HCV Exchange Clinic Registry was not existed in Kazakhstan. This makes an access to data difficult and does not allow for a comprehensive assessment of the prevalence proportion of viral hepatitis as well as the burden imposed on the public health system in the country[59].

According an independent study[60], conducted by the Research Institute of Cardiology and Internal Diseases of the Ministry of Health of the Republic of Kazakhstan in 2016 and 2017, the prevalence of HCV carriers ranged from 4.6% (South-Kazakhstan region) to 6% (Aktobe region).

The study included laboratory tests with the determination of total antibodies to the hepatitis C virus (AntiHCV) in blood, which required further confirmation by the PCR method.

HCV Exchange Clinic Registry was not existed



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According to the Statistics Committee of the Ministry of National Economy of Kazakhstan[61], the population of Kazakhstan was 18,415,500 as of February 1, 2019. Thus, the estimated number of people with antibodies to HCV can range from 850,000 to 1,105,000.

Below are the key statistics on viral hepatitis C provided by the Ministry of Health of the Republic of Kazakhstan[62]:

- number of people with HCV registered in 2017 - 19,938;
- number of HCV cases registered in 2017 - 4,297;
- prevalence of HCV (absolute number) - 24,235;
- prevalence of HCV (per 100 thousand population) - 134.4.

- number of people with HCV registered in 2018 - 24,063;
- number of people with HCV requiring treatment in 2018 - 18,684;
- as of 2018, a total of 4,996 HCV cases have been registered;
- prevalence of HCV (absolute number) - 29,099; and
- prevalence of HCV (per 100 thousand population) - 134.4.

[59]Resolution of the chief medical officers, the Workshop on Gastroenterology and Hepatology Issues, March 15, 2019.
[60]Journal «Medicine», No 9 (171), 2016, page 30-33 and No 5 (179), 2017, page 17-22.
[61]http://stat.gov.kz/faces/homePage?_afrLoop=4160784958148023#%40%3F_afrLoop%3D4160784958148023%26_adf.ctrl-state%3D1dtqvbru4f_4
[62]Letter of the Ministry of Health dated 02.02.2019, the Reference No 21-2-11/ZT-B399

Breakdown by years[63]:

Year 2017:
The total number of cases – 2 939:
Rate per 100,000 population – 16.22.

Year 2018:
The total number of cases – 3 213:
Rate per 100,000 population – 17.81.

Hepatitis C Antiviral Long- term Treatment

Since 2011, procurement of antiviral drugs for adults and children is provided entirely by public funds in Kazakhstan. Medical treatment of the citizens of Kazakhstan infected with HCV is carried out within the scope of the Statutory Free Medical Assistance / Compulsory Social Health Insurance (SFMA / CSHI).

OVERVIEW OF THE REGULATORY FRAMEWORK FOR HCV PREVENTION, DIAGNOSTICS AND TREATMENT

Since 2011, HCV prevention, diagnostics and treatment activities have been implemented in Kazakhstan in line with the following regulations:

1) Code of the Republic of Kazakhstan «On health of the population and the healthcare system» of September 18, 2009, No. 193-IV.
2) «Salamatty Kazakhstan» state healthcare development program for 2011-2015;
3) «Densaulyk» state healthcare development program for 2016-2019;
4) Guidelines for the Clinical Treatment of HCV in the Adults approved by the Joint Commission on the Quality of Healthcare Services of the Ministry of Health of the Republic of Kazakhstan of May 12, 2017, Minutes No. 22;
5) Order No. 92 of the Acting Minister of Health of the Republic of Kazakhstan «On Approval of the Rules for the Clinical Diagnostics and Treatment of Patients with Viral Hepatitis» of February 17, 2012;
6) Standard of the gastroenterological and hepatological care in the Republic of Kazakhstan;
7) State Sanitary Rules and Regulations "Public health requirements for sanitation and antiepidemic measures to prevent infectious diseases", Order No. 126 of the Acting Minister of Health of the Republic of Kazakhstan dated March 27, 2018;
8) Re Drug provision - the Order No. 666 of the Ministry of Health of the Republic of Kazakhstan dated by August 29, 2017, registered in the Ministry of Justice of the Republic of Kazakhstan on September 19, 2017 with the reference number 15724 «On approval of the List of medicines and medical products to provide citizens with free and (or) preferential medicines, medical products and specialized medical products on an outpatient basis in the framework of the system of statutory free medical assistance and the compulsory social health insurance, including certain categories of citizens with certain diseases (conditions)» (until 01.01.2018, the Order No. 786 of the Ministry of Health of Kazakhstan was used); (until 01.01.2018, the Order No. 786 of the Ministry of Health of Kazakhstan was used);
9) Order No. 451 of the Minister of Health of the Republic of Kazakhstan dated July 3, 2017. The Order was registered in the Ministry of Justice of the Republic of Kazakhstan on August 2, 2017 with the reference number 15417.

[63]Letter of the Scientific and Practical Center of Sanitary – Epidemiological Examination and Monitoring, 08/25 - 689 dated by Jan 30, 2019

Annex 6 containes table 6 with the list of registered medicines for the treatment of HCV in Kazakhstan". Source: The web-site of the National center for registration of drugs and medical devices of the MH RoK[64]; Kazakhstan National Drug Formulary (KNDF) of the MH RoK[65].

The latest "Clinical Protocol for the Treatment of Viral Hepatitis «C» in the Adults"[66], (hereinafter – the Protocol) was approved by the Joint Commission on the Quality of Healthcare Services of the Ministry of Health of the Republic of Kazakhstan on May 12th, 2017. The Protocol is going to be revised in 2019. The Protocol is based on the recommendations of the WHO, EASL[67], AASLD[68] provided in 2016. Tables 14, 15 and 16 below provide that the Protocol reflects virtually all the recommendations provided by the WHO in 2016 regarding the use of direct-acting antiviral agents in treating HCV, including a pangenotic (for all genotypes) regimen of HCV treatment such as the sofosbuvir and the daclatasvir.

According to the Order of the Ministry of Health[69], all citizens of Kazakhstan and equal-status persons have the right to free access to the sofosbuvir, daclatasvir and ribavirin regardless of the degree of severity. In this case, a patient must be clinically tracked by the medical institution.

Table 19. Indications for the Hepatitis C Antiviral Therapy

Order of priority	Group of patients	Strength of recommendations
Antiviral therapy is considered	• All patients with the compensated and de-compensated hepatic disorder who have or haven't previously received the treatment	A1
Antiviral therapy is strictly required	• F2-F4, including the de-compensated liver cirrhosis • Indications for a liver transplantation • HCV relapse after a liver transplantation • Clinically significant extrahepatic appearances, such as widespread vasculitis with HCV-associated diverse cryoglobulinemia • HCV-infected women who wish to recover before pregnancy • Hemodialysis patients • Health workers and other groups with the epidemiologically significant risk of transmission • Recipients of solid organs or stem cells • Concomitant diabetes	A1
Antiviral therapy may be delayed or assigned individually	• No fibrosis or mild fibrosis (F0-F1) in the absence of the above complicating factors	B1
Antiviral therapy is not recommended	• Patients with limited lifespan due to concomitant diseases not related to the liver	B2

[64]http://www.ndda.kz/
[65]http://www.knf.kz/index.php/kz/
[66]https://diseases.medelement.com/disease/%D1%85%D1%80%D0%BE%D0%BD%D0%B8%D1%87%D0%B5%D1%81%D0%BA%D0%B8%D0%B9-%D0%B2%D0%B8%D1%80%D1%83%D1%81%D0%BD%D1%8B%D0%B9-%D0%B3%D0%B5%D0%BF%D0%B0%D1%82%D0%B8%D1%82-%D0%B2-%D1%83-%D0%B2%D0%B7%D1%80%D0%BE%D1%81%D0%BB%D1%8B%D1%85/14152
[67]The European Association for the Study of the Liver
[68]The American Association for the Study of Liver Diseases
[69]The Order No.666 of the MH of RoK dated by August 29, 2017.

The Protocol consists of 16 regimens of the HCV antiviral therapies, including the pangenotypical scheme of sofosbuvir and daclatasvir.

The full text of the Protocol with the list of the HCV medical treatments could be found at the link above.

Table 20. Treatment regimens for patients with the HCV genotype 1a who have not previously received the treatment

Regimens	Group of patients	Having no cirrhosis	With compensated cirrhosis	With de-compensated cirrhosis
Preferable HCV regimens	LED/SOF	12 weeks	12 weeks	24 weeks or + RBV 12 weeks
	OMB/PAR/RIT+ DAS1	+ RBV 12 weeks	+ RBV 24 weeks	Not approved
	SOF/VEL*	12 weeks	12 weeks	24 weeks or + RBV 12 weeks
	SOF*+DCV*	12 weeks	24 weeks or + RBV 12 weeks	24 weeks or + RBV 12 weeks
	EBR/GZR*	± RBV12-16 weeks 2	± RBV12-16 weeks 2	Not approved
Alternative HCV regimens	SOF*+SMV	12 weeks	± RBV 24 weeks	Not approved
	SMV+Peg-IFNα+ RBV	24 weeks 3	48 weeks 3	Not approved
	SOF*+Peg-IFNα+ RBV	12-24 weeks 4	24 weeks	Not approved
	Peg-IFNα+RBV	24-72 weeks 5	48-72 weeks 5	Not approved

Table 21. Treatment regimens for patients with the HCV genotype 2 who have not previously received the treatment

Regimens	Group of patients	Having no cirrhosis	With compensated cirrhosis	With de-compensated cirrhosis
Preferable HCV regimens	**SOF*+DCV***	12 weeks	24 weeks or + RBV 12 weeks[1]	24 weeks or + RBV 12 weeks
	SOF/VEL*	12 weeks		24 weeks or + RBV 12 weeks
Alternative HCV regimens	SOF*+RBV	12 weeks[2]	24 weeks	24-48 weeks
	Peg-IFNα+RBV	24-48 weeks[3]	24-48 weeks[3]	Not approved

Table 22. Treatment regimens for patients with the HCV genotype 3 who have not previously received the treatment

Regimens	Group of patients	Having no cirrhosis	With compensated cirrhosis	With de-compensated cirrhosis
Preferable HCV regimens	**SOF*+DCV***	12 weeks	+ RBV 24 weeks	+ RBV 24 weeks
	SOF/VEL*	12 weeks	24 weeks or + RBV 12 weeks	+ RBV 24 weeks
Alternative HCV regimens	LDV/SOF	+ RBV 24 weeks	+ RBV 24 weeks	Not approved
	SOF*+RBV	24 weeks	Not approved	Not approved
	SOF*+Peg-IFNα+ RBV	12 weeks[1]	12 weeks[1]	Not approved
	Peg-IFNα+RBV	24-72 weeks[2]	48-72 weeks[3]	Not approved

ANALYSIS OF PURCHASES OF DRUGS TO ADDRESS HCV TREATMENT IN 2018

In 2017, 2,260.4 million tenge was allocated from the national budget for the treatment of hepatitis B and C types. However, it is not possible to get a detailed breakdown of the funding allocated for the treatment of the hepatitis C in 2017 due to the lack of data in official sources. 2,271.2 million tenge was allocated to purchase drugs for the treatment of hepatitis B and C in 2018. Starting from 2018, medical drugs will be dispensed at an outpatient level through the electronic DSIS program[70]. According to SK-Pharmacy LLP, prescription drugs for the treatment of hepatitis B and C in the amount of KZT 506, 2 million were dispensed in 2018.

In 2018, the HCV drugs were procured by the Single Distributor using only 1 method - through UNDP[71].

In accordance with subparagraph 6) of paragraph 314 of the Guidelines for the Procurement of Drugs and Medical Products approved by the Government of the Republic of Kazakhstan dated October 30, 2009 № 1729 ЛС (hereinafter referred to as Guidelines), a Single Distributor purchases drugs through international organizations incorporated by the United Nations agreement with an authorized body in health care, on the basis of the international treaties (agreements) ratified by the Republic of Kazakhstan, and the international treaties signed for the implementation thereof, through single source.

Sofosbuvir and Daclatasvir were procured through the UNDP Kazakhstan under the tender procurement and in the frame of the «Purchase of medicines for the treatment of socially significant diseases» project on February 1, 2018[72].

According to the Code of the Republic of Kazakhstan «On health of the population and the healthcare system», the procedure for importing drugs and medical products into the Republic of Kazakhstan is determined, inter alia, as follows:[73]

1. Drugs and medical products are imported into the Republic of Kazakhstan in the manner determined by a competent authority, in accordance with the customs legislation of the Republic of Kazakhstan and (or) the Eurasian Economic Union;

[70]The Drug Supply Information System
[71]United Nations Development Program
[72]http://procurement-notices.undp.org/view_notice.cfm?notice_id=44544
[73]Code of the Republic of Kazakhstan «On health of the population and the healthcare system», Article 80 - The procedure for importing medicines and medical devices into the territory of the Republic of Kazakhstan

3. Medical drugs and medical products that are not registered in the Republic of Kazakhstan may be imported to the Republic of Kazakhstan on the basis of a statement (authorization document) issued by an authorized body where they are intended for: 8) procurement by a single distributor of medical drugs and medical products supplied by international organizations established by the United Nations General Assembly, and (or) prequalified by the World Health Organization, with the exception of medical drugs and medical devices under long-term medical drugs and medical products supply contracts.

According to the Order No. 451[74], HCV is a socially significant disease. Below is a table of all antiviral drugs for the treatment of HCV, purchased by a Single Distributor in 2018.

Table 23. Antiviral drugs purchased by the SD through UNDP in 2018

INN	DOSAGE FORM	BRAND NAME	PACKING	NUMBER OF UNITS	NUMBER OF PACKAGES	SUPPLIER
SOFOSBUVIR 400 mg	tablet	MYHEP	28	1,550,640	55,380	UNDP
DACLATASVIR 60 mg	film coated tablet	MyDekla	28	1,550,640	55,380	UNDP

Table 24. The share of each drug in the total budget

INN	BRAND NAME	MANUFACTURER	NUMBER OF UNITS	AMOUNT AT SUPPLIER PRICE, KZT	AMOUNT AT SUPPLIER PRICE, USD	SHARE OF TOTAL PURCHASE (%)
SOFOSBUVIR 400 mg	MYHEP	MYLAN	1,550,640	614,348,061.60	1,649,880.96	100%
DACLATASVIR 60 mg	MyDekla	MYLAN	1,550,640	00	00	100%

In accordance with the annex to the order of the Minister of Health of the Republic of Kazakhstan dated August 22, 2017 No. 631 "On approval of the list of medical drugs and medical products as part of the statutory free medical assistance in the compulsory social health insurance system, procured from the Single Distributor for 2018", 1 tablet of Daclatasvir is additionally provided with each unit of Sofosbuvir[75].

Table 25. Cost analysis per unit, per package, per patient (12 weeks course of treatment)

INN	BRAND NAME	PACKING	UNIT KZT/USD	PACKAGE, KZT/USD	TREATMENT COURSE FOR 1 PATIENT, KZT/USD
SOFOSBUVIR 400 mg	MYHEP	28	346.19 / 1.064[76]	9,693.32 / 29.79	29,076.96 / 89.37
DACLATASVIR 60 mg	MyDekla	28	00	00	0

[74] Order №451 of the Ministry of Health of the Republic of Kazakhstan dated July 3, 2017.
[75] Letter of the Pharmacy Committee of the MOH RK dated 26.06.2018 № 3Т-Б-143; Letter of the Pharmacy Committee of the MOH RK dated 07.02.2019 № 3Т-Б-347
[76] At the rate of the 100% prepayment date, April 4th,2018; 1 USD = 325.37 tenge.

Table 26. Antiviral drug purchased by SD from a domestic manufacturer for 2018

INN	DOSAGE FORM	BRAND NAME	PACKING	NUMBER OF UNITS	NUMBER OF PACKAGES	SUPPLIER
RIBAVIRIN 200 mg	Film coated tablet	RIVIRIN	30	191,640[77]	6,388	Abdi İbrahim Global Pharm,LLP

Table 27. Cost analysis for the Ribavirin per unit, per package, per patient (12 weeks course of treatment).

INN	BRAND NAME	PACKING	UNIT KZT/USD	PACKAGE, KZT/USD	TREATMENT COURSE FOR 1 PATIENT, KZT/USD
RIBAVIRIN	RIVIRIN	30	34.13 / 0.09[78]	1023.00 / 2.76	2866.92 / 7,75

COMPETITION IN THE COURSE OF BIDDING

At the end of 2017, in order to expand access to the treatment by reducing the cost of HCV therapy, the AGEP'C Public Foundation appealed to the UNDP Kazakhstan to assist with the purchase of antiviral drugs. For 4 months, hard work was carried out to study the situation and legal documents. This was due to the fact that, as of 2017, the Sofosbuvir was under patent protection, and Kazakhstan was not part of the Gilead's voluntary license.

After a full analysis of the situation and the examination of all documents, and before the bidding, the UNDP Kazakhstan offered an initial price of USD 384 for a course of HCV treatment (12 weeks).

Subsequently, an appeal was forwarded to the Minister of Health of the Republic of Kazakhstan with the information about the price and a request to support the project on expanding access to treatment through the procurement of HCV drugs through an international organization. The Minister of Health, E.A. Birtanov, supported this proposal by instructing the Committee of Pharmacy of the MOH RK and the SD to examine it. On February 1, 2018, the Ministry of Health had signed a cooperation agreement with the UNDP as part of the "Procurement of medicines for the treatment of socially significant diseases" project dated February 1, 2018.

As a result of procurement in 2018:

1. Sofosbuvir drug was purchased 91% below the marginal price of the MH of RoK;
2. Savings amounted to KZT 1,4 billion compared with the marginal price of the MH of RoK;
3. The cost of treating one patient per year had dropped from USD 5,757 in 2017 to USD 89 in 2018.
4. In 2018, due to the savings, patients' coverage with antiviral drugs had increased from 4,000 to 18,684;
5. Coverage with treatment increased from 1,200 patients in 2011 to 18,684 patients in 2018.

[77] Letter of the Pharmacy Committee of the MOH RK dated 07.02.2019 № 3Т-Б-347
[78] 1 USD = 370 tenge

INTERRUPTIONS

There is a feedback system on http://www.hepatit.kz/ and on FB page[79]. There is also an electronic referral system on the website https://pereboi.kz/. All these methods are created and intended to collect information about the absence and interruption of vital drugs for the treatment of socially significant diseases, including HCV, by combined community efforts.

The appellant may leave information about the following:

- no HCV drugs were administered;
- the therapeutic regimen was suddenly changed;
- medical drugs were provided for a shorter period than normal; and
- no laboratory and instrumental diagnostics were provided as part of the Statutory Free Medical Assistance (SFMA)/ Compulsory Social Health Insurance (CSHI).

Information left using any of the above methods is received by the consultant. The consultant is a representative of the patient community and is not a healthcare facility worker. The consultant reports an incident to the representative of a competent authority of the Ministry of Health of the Republic of Kazakhstan.

In 2017, due to the existing priorities in the prescription of antiviral therapy, where first of all, the therapy was prescribed to patients with F3-F4 stage fibrosis, cirrhosis; inquiries came from patients with fibrosis with a stage up to F3, asking why they were denied therapy. In this case, enlightening talks were conducted with these patients concerning the rules of the AVT prescription.

There were also reports about denials of free-of-charge diagnostics, both during the next examination and during the AVT prescription. In such cases, the inquiring patients were provided with information about their right to free diagnostics, including its expensive types. In order to address these issues, the information was also conveyed to the heads of health care organizations and heads of health care facilities of cities and regions.

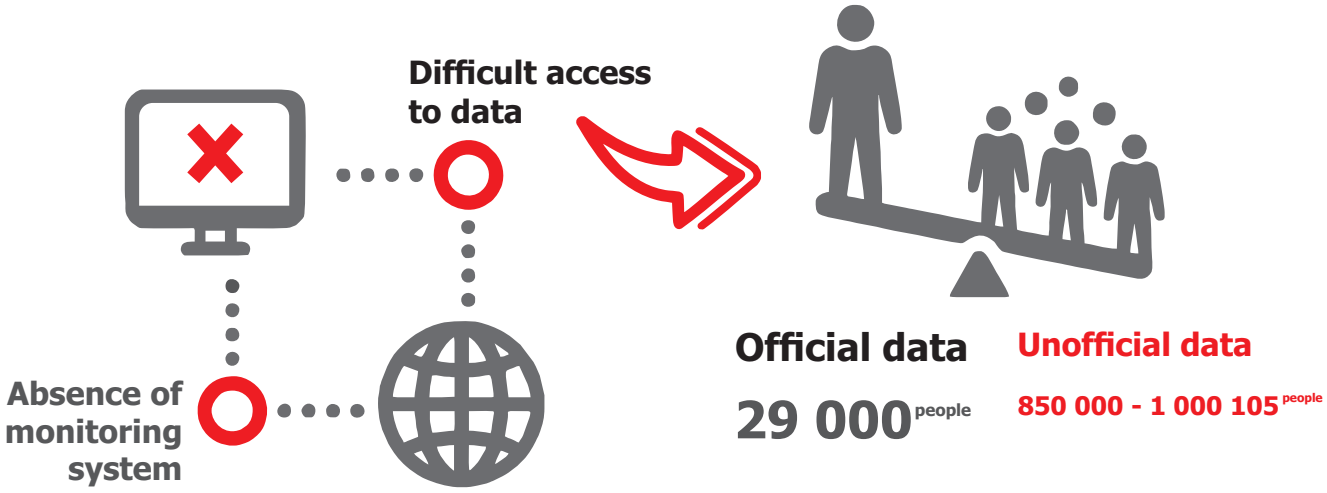
Since the beginning of 2018, due to the long period of procurement and supply of antiviral drugs through an international organization, reports concerned the absence of antiviral drugs in medical organizations. Before the receipt of drugs, explanatory work was conducted (through personal correspondence and through social media) as to why there are no drugs, and why this is done. Upon receipt of drugs, all patients were fully provided with them.

In order to address the issues, information was also conveyed to the heads of medical organizations, heads of health facilities of cities and regions.

[79]https://www.facebook.com/agepckz/)

KEY FINDINGS

1. Access to the data on the prevalence of HCV in Kazakhstan is inhibited due to the fact that there is no well-established monitoring system. According to official data, in 2018 about 29 thousand people were diagnosed with HCV. According to estimates, the number of people with antibodies to HCV may vary from 850 thousand to 1 million 105 thousand; however, these figures need to be adjusted.



2. In 2011, in the Republic of Kazakhstan, the procurement of antiviral drugs for adults and children is enshrined entirely by public funds. Medical assistance to the citizens of the Republic of Kazakhstan infected with HCV is provided as part of the statutory free medical assistance.

3. Based on procurement data, in 2018, 18,864 patients with a confirmed HCV diagnosis and registered as on 01.01.2018 were provided with a pangenotypic HCV treatment regimen using Sofosbuvir and Daclatasvir drugs. The percentage of treatment coverage of the number of patients, subject to regular medical check-up as on 01.01.2018 was 100%.

4. The price of a single patient 12 weeks' treatment course for a standard treatment regimen was USD 89, which is one of the lowest in the world. According to the Pharmacy Committee of the MH RK, Sofosbuvir and Daclatasvir were procured for USD 376,809.2.

5. The latest clinical treatment protocol for viral hepatitis C in adults dated May 2017 contains all antiviral drugs on the market and complies with the WHO recommendations. Revision is scheduled for 2019.

RECOMMENDATIONS FOR THE HCV TREATMENT DRUGS

1. Launch of the viral hepatitis C and B testing program for the population of the Republic of Kazakhstan as recommended by the WHO.

2. Launch of the National Registry of patients with viral hepatitis.

3. Expanding the use of other viral hepatitis C treatment regimens for certain groups of patients who Sofosbuvir and/or Daclatasvir are contraindicated, including children less than 12 years of age. Work to improve the availability of other therapeutic regimens, including the Sofosbuvir/Velpatasvir and the Glecaprevir/Pibrentasvir pangenotypic schemes.

4. Subsequent expansion of antiviral therapy coverage in accordance with the recommendations.

FOCUS AREAS IN THE FUTURE

1) Promotion of the WHO recommendations[80] on universal testing of citizens for viral hepatitis "C" and "B".

2) Expansion of the list of outpatient care and pharmaceutical benefits.

3) Ensuring further reduction in the cost of antiviral drugs used in the HCV/HBV treatment.

4) Continuing work with the Republican E-Health Center on the introduction of a VH web registry.

5) Update of the clinical protocol on "Chronic Hepatitis C in Adults" in 2019.

6) Expanded coverage of the newly identified patients with essential medical drugs, including other treatment regimens.

7) Address the issue of Glecaprevir/Pibrentasvir drug:
- inclusion of the Republic of Kazakhstan in the existing License; and
- consideration of the issuing a compulsory license.

[80] WHO Guidelines on Hepatitis B and C Testing, February 2017

INTELLECTUAL PROPERTY BARRIERS, PREVENTING ACCESS TO GENERIC PRODUCTS IN KAZAKHSTAN

DRUG PATENT AND CONTESTATION OF THE PATENT

A patent certifies the priority, authorship and exclusive right to a patented drug. The scope of legal protection provided by a patent for a drug is determined by a formula. The description and drawings may be used to interpret the formula.

Medical drug patenting procedure:

Patents are issued by the National Institute of Intellectual Property of the Ministry of Justice, while the role of the MoH in the patent granting procedure is not formalized in legislation.

On the application submitted to the expert organization, the date of filing of the application is established. After establishing the filing date of the patent application for an invention, the expert panel conducts the examination as to form thereunder (verification of the presence and compliance of the documents).

After completion of the examination as to form of patent with a positive outcome, the expert panel examines the application as to substance.

Examination of the application as to substance includes determination of the possibility of classifying the application as already existing patents and a search is made to determine compliance with the patentability criterion[81]. In case of proof of the patentability criteria, a patent is granted for an invention.

The decision to deny a patent is made in the following cases:

1) Where the application is related to the objects not protected as inventions;
2) Where additional documents contain formulas, different from the original application.
3) In case of failure to submit additional or corrected documents.

The accelerated expert examination of objects for which favorable conditions for patenting are provided for, includes the following actions conducting within six months:

1) Expert examination as to form;
2) Information retrieval; and
3) Expert examination as to substance.

The list of objects for which favorable patenting conditions are provided is determined by a competent authority.

The expert panel performs registration in the relevant state registers:

1) Issuance of title documents, and open or forced license;
2) Transfer of the exclusive right to use the object of industrial property;
3) Granting the right to use the industrial property;
4) Early termination or invalidation of the granted patent.

The relevant state registries are posted on the website of the expert panel. After the publication of the information on the issuance of a document of title, any person has the right to review the application materials and the information retrieval report prepared by the expert panel.

[81] Established by Article 6 of this law

Term of the patent and the possibility to extend it

The patent for the medical drug is valid for twenty years from the date the application is filed and can be extended for five years. This period will be extended by the time elapsed from the application for patent is filed to the date of receipt of the first permit to use the invention, minus five years.

The patent granted for the process for obtaining a product extends to the product obtained using this process.

The right to obtain a patent, holding it and the exercise of rights that a patent implies may be transferred in whole or in part to another person.

Patentability Requirements

Legal protection is granted over the medical drug, where it is new, has an inventive step and is industrially applicable (can be used in healthcare). The patent holder has the exclusive right to use the protected medical drug at their discretion, from the date of publication in the official information bulletin.

The use of the medical drug includes the manufacture, use, import, offer for sale, sale, other commercialization or storage of the medical drug for this purpose, as well as the use of the protected process for its production.

The following are not recognized as inventions:

1) discoveries, scientific theories and mathematical methods;
2) business and organization methods;
3) symbols, schedules and rules;
4) rules and methods of mental operations and conducting games;
5) programs for computers and algorithms as such;
6) projects and layouts for structures, buildings and territories;
7) proposals relating only to the product appearance; анв
8) proposals contrary to public order, principles of humanity and morality.

terms of patent issuing

In general, the procedure for granting patents meets the provisions of the Trade-Related Aspects of Intellectual Property Rights (TRIPS). However, the terms for issuing a patent and a list of things for which a patent cannot be obtained do not contribute to the interests of patients. In particular, TRIPS does not contain recommendations to extend the period by more than 20 years, and an extension for an additional 5 years looks like an opportunity for manufacturers of original drugs to maintain a monopoly in the market.

In the list of items not recognized as inventions there are no such items as **a new use of already known medicines, minor improvements, a new form of application, and new methods of treatment.** This contributes to the emergence of secondary patents that extend the term of patent protection, which also contributes to the monopoly of original manufacturers.

Disputing a patent

A patent during the entire term of validity may be disputed and invalidated in whole or in part due to a challenge thereto in the following cases:[82]

1) Non-compliance with the patentability requirements.

Invalidation of a document of title and early termination thereof

A patent is declared invalid in whole or in part on the basis of a court ruling and is revoked from the date patent application is filed, and the entry in the relevant state register is also canceled.

In the event that the document of title is partially invalid, a new patent is issued for the remaining protectable subjects.

Licensing agreements signed on the basis of a patent that was subsequently invalidated shall remain valid to the extent they were executed at the time of the ruling invalidating such a patent.

2. The document of title is terminated early in the following cases:

1) on the basis of the application filed by the patent owner to the authorized body, from the date of publication of information about the early termination of the title of protection in the bulletin. If the document of title is issued for a group of industrial property objects, and the patent owner's application is submitted for only part of this group of objects, the document of title is terminated only for industrial property objects indicated in the application.

2) in case of non-payment of the document of title in force from the date of expiration of the established payment term, within the established time period.

3) The expert organization publishes in the bulletin information that the document of title was recognized as invalid, or that the validity of the document of title was terminated early.

Re-entry of patent into force and right of posterior use

1) In the event that a patent is suspended due to late payment, the patent holder may renew the patent upon a motion, by making payment. Information about re-entry of a patent into force must be published within 2 months. Date of publication is the date of re-entry of the patent into force.

2) Any person who, during the period of suspension of the patent, began using the patented item in the territory of the Republic of Kazakhstan, or made the necessary preparations for this, retains the right to continue using it free of charge without expanding the scope of such use (Right of Posterior Use).

[82]Patent Law of the Republic of Kazakhstan dated July 16, 1999 No. 427, Pharagraph 7 Article 33

The right of after-use can be assigned to another person only in conjunction with the production where the patented item was used or preparations necessary for this have been made.

Disputes consideration procedure

The following disputes are subject to review in court:

1) On the authorship of industrial property;

2) On the legality of document of title;

2-1) On invalidation of a patent;

3) On the establishment of the patent owenership;

4) On issuance of a forced license;

5) on violation of the exclusive right to use the protected object of industrial property and other property rights of the patent owner;

6) on the conclusion and execution of licensing agreements for the use of a protected industrial property object;

7) On the right of prior use and posterior use;

8) about the remuneration of the author by the employer;

9) on payment of compensations provided by this Law;

10) Other disputes related to the protection of rights arising from the document of title.

The following shall be subject to judicial review, and may also be reviewed through arbitration or mediation by agreement of the parties:

- On the infringement of the exclusive right to use the protected item and other property rights of the patent holder;
- On the execution and performance of license agreements for the use of a protected item;
- On payment of remuneration to the author by employer; and
- On payment of compensation fees provided for by this law.

Patent rejection claims are filed to court after the review of the relevant objections in the board of appeal.

On the basis of a court ruling, the expert panel publishes the information about any changes in the title documents.

The patent holder has the right to assign the exclusive right held by them to the patented item to another individual or legal person under an assignment agreement.

The assignment of the exclusive right to the patented item is subject to registration in the relevant state register.

Prior-use right and temporary legal protection

A person who, before the priority date[83] of the patented item, had conscientiously used in the territory of RK a solution similar to the patented item that was created independently of the author or made the preparations necessary for this, retains the right to its royalty-free use without expanding the scope of such use (right of prior use).

The right of prior use may be assigned to another person only in conjunction with the production where the use of the identical solution took place or the necessary preparations were made for this.

Open License

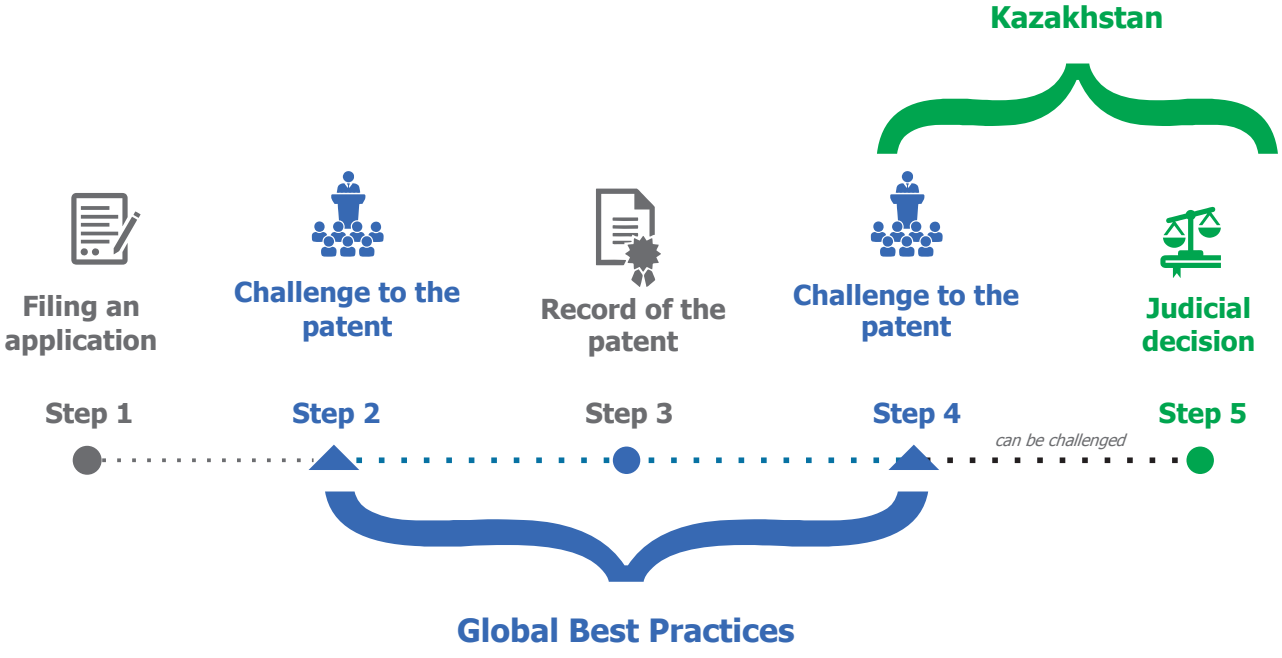
The patent holder may submit an application to the expert panel for granting the right to use the patented item to any person (open license).

The application of the patent holder on granting the right to an open license may not be revoked and remains valid for three years from the date of its registration. The granting of the right to an open license is subject to registration within one working day from the date of receipt of the application from the patent holder or a party concerned, with the necessary documents attached.

Infringement of the exclusive rights of the patent holder

Infringement of the exclusive rights of the patent holder is unauthorized manufacture, use, import, storage, offer for sale, sale and other commercialization of a product created using a patented process (production process), or commercialization of a product manufactured in a directly protected procedure.

The legislation of Kazakhstan provides for the possibility to raise objections «against» the granting a patent during the entire period of its validity. The procedure for challenging a patent «after» its issuance provides for litigation, which can last for years. It would be more expedient to prevent the patenting of new drugs, the patentability of which is in doubt, at the stage of consideration of the application for registration of a patent, that is, "before" its registration.



[83]https://www.wipo.int/sme/ru/faq/pat_faqs.htm

FORCED NON-EXCLUSIVE LICENSE

If the patent holder does not use the industrial property and refuses to enter into a license agreement on acceptable commercial terms within ninety calendar days from the date of the inquiry, any person may apply to court for a compulsory non-exclusive license where the industrial property was not continuously used after the first publication of the information on the issuance of a security document to an industrial property during any three years preceding the date of such an application.[84]

If a patent holder fails to prove that such failure to use is due to legitimate reasons, the court grants the above license specifying the scope of use, terms, amount and payment procedure. The amount of payments must not be below the market price of the license, determined in accordance with the established practice.

Forced non-exclusive license (FNEL) is granted in the following cases[85]:

1) Failure of the patent holder to use the patented item and refusal to enter into a licensing agreement on acceptable commercial terms within ninety calendar days from the date of the inquiry, any person may apply to court for a forced non-exclusive license where the industrial property was not continuously used after the first publication of the information on the issuance of a document of title to the industrial property during any three years preceding the filing date of such an application.

   If the patent holder fails to prove that such failure to use is due to legitimate reasons, the court grants the above license specifying the scope of use, terms, amount and payment procedure. The amount of payments must not be below the market price of the license, determined in accordance with the established price.

2) The need to ensure national security or public health;

3) Abuse by the patent holder of their exclusive rights, promotion or failure to prevent such abuse of such exclusive rights by another person with their consent.

Any FNEL must be issued primarily to meet the demands of the domestic RK market, unless such a license is requested for the medical drug or the manufacturing process of the medical drug for the purpose of exporting the patented medical drug, or of the medical drug obtained through the patented process to a territory that does not have or lacks a sufficient amount of production facilities, in accordance with the international treaties ratified by the Republic of Kazakhstan.

The right to use a patented item may only be assigned by a person who has been granted a CNEL, to another person in conjunction with the corresponding production in which this item is used.

FNEL may be canceled by a court in case of termination of the circumstances that was the reason for its issuance.

Issuing FNEL automatically cancels the validity of the exclusivity of the registration dossier.

[84]Patent Law of the Republic of Kazakhstan dated July 16, 1999 No. 427, part 4 of article 11
[85]Patent Law of the Republic of Kazakhstan dated July 16, 1999 No. 427, part 4 of article 11

A patent holder who cannot use an industrial property without infringing on the rights of another patent holder who has refused to enter into a licensing agreement on acceptable commercial terms has the right to apply to a court for a license for the use of a patented item in the territory of the Republic of Kazakhstan.

If a patent holder who cannot use an industrial property without infringing on the rights of the holder of another document of title, can prove that their industrial property is an important engineering achievement and is of great economic importance to the industrial property of the holder of another document of title, the court may make a judgment to grant them a forced non-exclusive license.

When granting the above license, the court must determine the scope of use of the industrial property, for which the document of title is held by another person, the terms, amount and procedure of payments. The amount of payments must not be below the market price of the license, determined in accordance with established practices.

The right to use an industrial property obtained on the basis of this clause may only be transferred in conjunction with the assignment of a document of title to the industrial property in connection with which this right is granted.

In case of obtaining a forced license, the holder also has the right to obtain a license to use the sub-invention, in connection with which the compulsory license was granted.

The forced license is one of the TRIPS flexible provisions tools, which allow increasing the number of patients' access to the newest drugs for treating HIV at the significant price reduction. Unfortunately, the legislation of Kazakhstan considers only one of the existing options for issuing a forced license - through the litigation with the patent owner, while in patient-centered countries other options are also provided, such as issuing a forced license by the patent office in consultation with the Ministry of Health, with appropriate justification for expediency.

Law Enforcement Practice: https://informburo.kz/novosti/britanskiy-postavshchik-otkazal-kazahstanu-v-skidke-na-preparat-dlya-pacientov-s-vich.ht ml
http://itpcru.org/2016/07/01/modelnyj-isk-o-vydache-prinuditelnoj-litsenzii-na-arv-v-kazahstane/

PARALLEL IMPORTING

Medical drugs are imported into the territory of the Republic of Kazakhstan in the manner determined by a competent authority in accordance with the customs legislation of the Republic of Kazakhstan and (or) the Eurasian Economic Union[86].

Importation into the territory of the Republic of Kazakhstan of the medical drugs, which did not undergo state registration in the Republic of Kazakhstan, is not allowed, except for the following cases[87]:

1) conducting clinical trials;

2) expert examination of medical drugs and medical devices during state registration, re-registration, and amendments to the registration dossier;

3) performing state registration of medical drugs and medical devices;

4) medical care to a particular patient according to vital indications, or medical care provided to a limited number of patients with rare and (or) very severe pathology with the possible medical use and procurement;

5) holding exhibitions without the right to their subsequent sale;

6) prevention and (or) elimination of emergency consequences;

7) introduction of innovative medical technologies;

8) procurement by a single distributor of medical drugs and medical devices supplied by international organizations incorporated by the United Nations General Assembly, and (or) prequalified by the World Health Organization, with the exception of medicines and medical devices under long-term contracts for the supply of medical drugs and medical products;

9) use as an accessory, that is part of a medical device and not intended for independent use outside the medical device.

Drugs and Medical Products (Including Unregistered), intended for humanitarian aid (assistance) or assistance in emergencies, are imported into the Republic of Kazakhstan on the basis of a report (permit) granted in the manner determined by a competent authority.

Medical drugs and medical devices imported into the territory of the Republic of Kazakhstan that do not meet the requirements of the legislation of the Republic of Kazakhstan in the field of health care are subject to confiscation and destruction.

Persons who are allowed to import medicines and medical devices into the territory of the Republic of Kazakhstan.

The import of medical drugs and medical products into the territory of the Republic of Kazakhstan in the manner determined by a competent authority can be performed by:

1) entities in the field of circulation of medical drugs and medical devices that are licensed to manufacture medicines and medical devices;

[86]Code of the Republic of Kazakhstan «On health of the population and the healthcare system», Art. 80
[87]Code of the Republic of Kazakhstan «On health of the population and the healthcare system», Art. 80

2) entities in the field of circulation of medical drugs and medical devices that are licensed to wholesale the sale of medicines or are included in the register of healthcare entities engaged in the wholesale sale of medical devices, upon notice of the commencement of activities;

3) research organizations, laboratories for the development and state registration of medicines and medical devices in accordance with this Code;

4) foreign manufacturers of medical drugs and medical devices, their authorized representative offices (branches) or their trusted individuals and legal entities for expert examination at the time of state registration, clinical trials and (or) studies and for participation in exhibitions of manufacturers of medical drugs and medical devices in the Republic of Kazakhstan;

5) healthcare organizations for medical activities.

The topic of parallel imports in Kazakhstan concerns the principle of the exhaustion of **trademark rights.**

Various graphic, verbal, alphabetic, numeric, three-dimensional and other marks or their combinations can be registered as a trademark[88].

A trademark can be registered in any color or color combination[89].

The owner of the trademark has the exclusive right to use and dispose of his trademark in relation to the goods and services specified in the certificate[90]. No one can use[91] a trademark protected in the Republic of Kazakhstan without the owner's consent.

It is not a violation of the exclusive right to a trademark to use this trademark in relation to goods that were legally entered into circulation on the territory of any of the member states of the Eurasian Economic Union directly by the owner (rightholder) of the trademark or by other persons having his consent[92].

Thus, Kazakhstan has a regional principle of the exhaustion of trademark rights, implying the circulation of goods within the EAEU.

According to the regional principle of exhaustion of rights, the Republic of Kazakhstan can deliver the drug to the territory of Kazakhstan from a country located on the territory of the Eurasian Economic Union, using the price set in that country and fixed by the holder of the right to the original drug.

The international practice of international exhaustion of rights allows importing products from any country in the world where the right holder has already introduced his product to the market using the same price as the right holder in that country has set. Considering the difference in prices in countries with different income levels, this change in the legislation of Kazakhstan will significantly reduce budget expenditures on the purchase of original drugs.

[88]Law of the Republic of Kazakhstan dated July 26, 1999 No. 456-I "On Trademarks, Service Marks and Appellations of Origin of Goods" (with amendments and additions as of January 21, 2019) Chapter 2, Article 5.
[89]Information Letter No. 95 of the National Patent Office under the Cabinet of Ministers of the Republic of Kazakhstan dated January 19, 1995.
[90]Law of the Republic of Kazakhstan dated July 26, 1999 No. 456-I "On Trademarks, Service Marks and Appellations of Origin of Goods" (with amendments and additions as of January 21, 2019) Chapter 2, Article 4.
[91]The use of a trademark or appellation of origin of goods is the placement of a trademark or appellation of origin of goods on goods and in the provision of services in respect of which they are protected on their packaging, production, use, import, storage, offer for sale, sale of goods with the designation trademark or appellation of origin, use in signage, advertising, printed matter or other business documentation, as well as their other introduction into circulation;
[92]Law of the Republic of Kazakhstan dated July 26, 1999 No. 456-I "On Trademarks, Service Marks and Appellations of Origin of Goods" (with amendments and additions as of January 21, 2019) Article 43

DATA EXCLUSIVITY

The National Centre for Expertise of Drugs, Medical Products and Medical Equipment does not allow, without the applicant's consent, to disclose and use for commercial purposes the confidential information provided for the state registration of the medical drug, contained in the application for state registration, the expertise of the medical drug, as well as the registration dossier of the medical drug, containing new chemicals, for six years from the date of state registration of the medicine[93].

These clauses of the provision preventing non-disclosure and commercial use of confidential information do not apply to:

1) the individual or entity who have been issued a forced license to use a medicinal product in accordance with the Patent Law of the Republic of Kazakhstan[94].

2) the use, production, import, export or distribution of a medical drug for non-commercial purposes.

On the basis of a court ruling, the disclosure and use of information are permitted without the consent of the applicant, in one of the following cases:

1) where the supply of the medical drug is insufficient to meet the needs of the population within twelve months from the date of registration in the Republic of Kazakhstan;

2) there is a need to protect public health in emergencies in order to ensure national security;

3) in order to identify actions that violate the requirements of the competition legislation of the Republic of Kazakhstan.

The exclusivity of the data, in which the data on a new drug is closed within 6 years after patent registration, makes it impossible for other manufacturers to start developing generic versions of this new drug. The later generic companies start this work, the longer Kazakhstan patients will not see available drugs on the market.

It is advisable to abolish the "Exclusivity of Data" to expand available generic drugs, stimulate competition in the drug market, and expand treatment coverage for patients.

[93]Code of the Republic of Kazakhstan «On health of the population and the healthcare system» of September 18, 2009, No. 193-IV, Art. 19.
[94]Code of the Republic of Kazakhstan «On health of the population and the healthcare system» of September 18, 2009, No. 193-IV

PATENT LINKAGE

The concept of "patent linkage" may include the following:

- providing information on the presence or absence of exclusive rights of third parties when applying for registration;
- verification of the medicines being registered in the Russian Federation for their use of patented inventions therein; and
- actions of the registration authority aimed at denial, suspension of registration, or other.

State registration of the reproduced medical drug is performed with the issuance of a marketing authorization certificate, without the right to sell the medical drug before the expiry of the document of title for the original medical drug.

The applicant informs in writing about non-infringement of the third party rights protected by a patent in connection with the registration of a medical drug[95].

The guidelines for expert examination of medical drugs: in the application for the expert examination of a medical drug, there is p 18: the presence of a document of title for an invention or utility model, or a trademark[96].

After registration, the party concerned receives the opportunity to first suspend the validity of the marketing authorization certificate, and then dispute it in court on the basis of an infringement of their exclusive rights.

In case of receipt by the "National Centre for Expertise of Drugs, Medical Products and Medical Equipment" of the information about any infringement on the exclusive rights of the document of title for invention in the field of drug circulation, the marketing authorization certificate is suspended until the results of the court proceedings are obtained on the basis of the following documents[97]:

1) an application of the patent holder of the document of title for an invention or utility model about the fact of infringement on its exclusive rights by another applicant or their representative;

2) a notarized copy of the patent for an invention or utility model; and

3) a court ruling on the assignment of case disputing (infringing on) the exclusive rights for judicial examination.

When a court ruling on infringement or non-infringement of exclusive rights by third parties comes into force, the government body revokes the marketing authorization or renews the marketing authorization[98].

[95]Order No. 523 of the Minister of Health and Social Development of the Republic of Kazakhstan dated June 26, 2015, Clause 11 on amending and supplementing the order of the minister of health of the Republic of Kazakhstan dated November 18, 2009 no. 735 "On approval of guidelines for state registration, reregistration and amendments to the registration dossier of medical drugs, medical devices and medical equipment".
[96]Order No. 736 of the Minister of Health of the Republic of Kazakhstan dated November 18, 2009, paragraph 18.
[97]Order No. 523 of the Minister of Health and Social Development of the Republic of Kazakhstan dated June 26, 2015. Clause 11-1 on amending and supplementing the order of the minister of health of the Republic of Kazakhstan dated November 18, 2009 no. 735 "On approval of guidelines for state registration, reregistration and amendments to the registration dossier of medical drugs, medical devices and medical equipment".
[98]Order No 106 of the Ministry of Health and Social Development of the Republic of Kazakhstan dated February 27, 2015

In case of withdrawal of marketing authorization, the National Centre for Expertise of Drugs, Medical Products, and Medical Equipment shall decide within five calendar days from the date of receipt of the information:

1) on the suspension of medical use of the medical drug by suspending the effect of the Marketing Authorization of the medical drug.

2) on the prohibition of medical use and withdrawal from circulation or suspension of medical use of a series (batch) of the medical drug.

This clause does not provide for the interests of patients living with HIV in terms of interruptions in treatment. When withdrawing a batch of drugs, it will be necessary to carry out all the procurement procedures, which for many ARV drugs take several months: http://almaty.sud.kz/rus/news/sud-vosstanovil-narushennye-isklyuchitelnye-prava-na-patent

BOLAR PROVISION

Actions that are not recognized as an infringement of the exclusive rights of the patent holder[99].

The following is not deemed to be an infringement on the exclusive rights of the patent holder:

2) conducting scientific research or experiment on a device containing a protected industrial property, where the purpose of such scientific research or experiment is not to generate income.

Рекомендации:

1. To limit the patent duration to 20 years without the option to renew.
2. To introduce the concept of challenging a patent "before" granting a patent.
3. In the event of the IP rights infringement claim from a patent holder, due to the form supply of generic drugs to ensure the statutory free medical assistance and CSHI, where there is a valid patent, to abolish the withdrawal of the lot received.
4. To introduce the concept of the "government use" - issuing a compulsory license for drugs on the basis of an order of the National Patent Office and the Ministry of Health, for the benefit of public health.
5. To apply the international exhaustion regimen for parallel importation procedures.
6. To eliminate the "Data Exclusivity" concept in order to stimulate the competitive environment and reduce the price of medicines, after expiration of the patent.

[99]Patent Law of the Republic of Kazakhstan dated July 16, 1999 No. 427, part 4 of article 12.

Annex 1

Table 6. List of registered ARV medicines in Kazakhstan[100]

No	Product licence number	Brand Name	Type	Date of Registr.	Manufacturer	ATC-code
1	RK-LS-5№020716	**Abacavir and Lamivudine**	Registration	23.07.2014	Aurobindo Pharma Limited	(J05AR02) Lamivudine and Abacavir
2	RK-LS-5№019939	**Abacavir USP tablets**	Registration	19.09.2018	Mylan Laboratories Limited	(J05AF06) Abacavir
3	RK-LS-5№023209	**Avonza**	Registration	05.09.2017	Mylan Laboratories Limited	(J05AR) Lamivudine/Tenofovir/Efavirenz 300 mg/300 mg/400 mg
4	RK-LS-5№016561	**Aluvia**	Re-registration	25.09.2015	AbbVie Deutschland GmbH & Co	(J05AR10) Lopinavir and Ritonavir
5	RK-LS-5№014087	**Aluvia**	Re-registration	07.10.2014	AbbVie Deutschland GmbH & Co. КГ	(J05AR10) Lopinavir and Ritonavir
6	RK-LS-5№121752	**Amiviren**	Registration	23.10.2015	JSC “Pharmasyntez”	(J05AF05) Lamivudine
7	RK-LS-5№121751	**Amiviren**	Registration	23.10.2015	JSC “Pharmasyntez”	(J05AF05) Lamivudine
8	RK-LS-5№022492	**Atazanavir and Ritonavir**	Registration	24.11.2016	Hetero Labs Limited	Combinations of antiviral drugs active against HIV
9	RK-LS-3№021526	**Virakar**	Registration	16.02.2018	Abdi Ibrahim Global Pharm	(J05AF06) Abacavir
10	RK-LS-5№005657	**Viramune**	Re-registration	23.12.2016	West-Ward Columbus Inc.	(J05AG01) Nevirapine
11	RK-LS-5№016270	**Viramune**	Re-registration	20.05.2015	Boehringer Ingelheim GmbH	(J05AG01) Nevirapine
12	RK-LS-5№020705	**Viread**	Registration	02.07.2014	Takeda GmbH	(J05AF07) Tenofovir disoproxil
13	RK-LS-5№015597	**Virokomb**	Re-registration	23.04.2015	Sun Pharmaceutical Industries Limited	(J05AR01) Zidovudine и Lamivudine
14	№ RK-LS-5№005491	**Virol**	Registration	14.08.2017	Sun Pharmaceutical Industries Limited	(J05AF06) Abacavir
15	RK-LS-5№016204	**Virolam**	Re-registration	25.09.2015	Sun Pharmaceutical Industries Limited	(J05AF05) Lamivudine
16	RK-LS-5№122110	**Darunavir-AIGF**	Registration	04.03.2016	Abdi Ibrahim Global Pharm	(J05AE10) Darunavir
17	RK-LS-5№122111	**Darunavir-AIGF**	Registration	04.03.2016	Abdi Ibrahim Global Pharm	(J05AE10) Darunavir
18	RK-LS-5№021638	**Dizaverox**	Registration	15.09.2015	JSC “Pharmasyntez”	(J05AR01) Zidovudine and Lamivudine
19	RK-LS-3№021498	**Duolazid**	Registration	23.04.2018	Abdi Ibrahim Global Pharm	(J05AR01) Zidovudine and Lamivudine

[100]List of registered drugs for 06.11.2017. Available at: http://www.dari.kz/category/search_prep, https://drugs.medelement.com

20	RK-LS-5№016700	**Zeffix**	Re-registration	19.11.2015	GlaxoSmithKline Inc.	(J05AF05) Lamivudine
21	RK-LS-5№003545	**Zeffix**	Re-registration	14.10.2015	GlaxoSmithKline Pharmaceuticals Ltd.	(J05AF05) Lamivudine
22	RK-LS-5№005698	**Ziagen**	Re-registration	02.12.2016	GlaxoSmithKline Pharmaceuticals Ltd.	(J05AF06) Abacavir
23	RK-LS-3№021549	**Zidoas**	Registration	15.06.2018	Abdi Ibrahim Global Pharm	(J05AF01) Zidovudine
24	RK-LS-5№021209	**Intelence**	Registration	03.03.2015	Janssen-Cilag Inc.	(J05AG04) Etravirine
25	RK-LS-5№014509	**Intelence**	Re-registration	18.07.2018	Janssen-Cilag Inc.	(J05AG04) Etravirine
26	RK-LS-5№021158	**Isentress**	Registration	26.01.2015	Pateone Pharmaceuticals Inc.	(J05AX08) Raltegravir
27	RK-LS-5№021157	**Isentress**	Registration	26.01.2015	Pateone Pharmaceuticals Inc.	(J05AX08) Raltegravir
28	RK-LS-5№020768	**Isentress**	Registration	02.09.2014	MSD International GmbH / MSD Ireland (Ballidin)	(J05AX08) Raltegravir
29	RK-LS-5№015503	**Kaletra**	Re-registration	14.05.2015	Aesica Queenborough Ltd.	(J05AR10) Lopinavir and Ritonavir
30	№ RK-LS-5№122110	**Kemeruvir**	Registration	04.03.2016	JSC “Pharmasyntez”	(J05AE10) Darunavir
31	№ RK-LS-5№122111	**Kemeruvir**	Registration	05.03.2016	JSC “Pharmasyntez”	(J05AE10) Darunavir
32	RK-LS-5№005697	**Kivexa**	Re-registration	24.01.2017	Glaxo Operations UK ltd, Glaxo Wellcome Opeations	(J05AR02) Lamivudine and Abacavir
33	RK-LS-5№010563	**Combivir**	Re-registration	23.10.2017	GlaxoSmithKline Pharmaceuticals Ltd.	(J05AR01) Zidovudine and Lamivudine
34	RK-LS-5№022580	**Complera**	Registration	26.12.2016	Pateone Inc.	(J05AR08) Emtricitabine, Tenofovir disoproxil and Rilpivirine
35	RK-LS-3№020658	**Lamias 150**	Re-registration	19.09.2017	Abdi Ibrahim Global Pharm	(J05AF05) Lamivudine
36	RK-LS-5№023212	**Lamivudine**	Registration	06.09.2017	Strides Shasun Limited	(J05AF05) Lamivudine
37	RK-LS-5№023000	**Lamivudine and Zidovudine**	Registration	25.05.2017	Strides Shasun Limited	(J05AR01) Zidovudine and Lamivudine
38	RK-LS-5№121913	**Lamivudine and Zidovudine**	Registration	14.12.2015	Mylan Laboratories Limited	(J05AR01) Zidovudine and Lamivudine
39	RK-LS-5№020710	**Lamivudine and Zidovudine**	Registration	15.07.2014	Aurobindo Pharma Limited	(J05AR01) Zidovudine и Lamivudine
40	RK-LS-5№020819	**Lamivudine and Tenofovir disoproxila fumarate**	Registration	24.09.2014	Aurobindo Pharma Limited	(J05AR) Antiviral drugs active against HIV, combinations

41	RK-LS-5№020717	**Lamivudine, Zidovudine and Nevirapine**	Registration	23.07.2014	Aurobindo Pharma Limited	(J05AR05) Zidovudine, Lamivudine and Nevirapine
42	RK-LS-5№021156	**Lamivudine/ Zidovudine Teva**	Registration	26.01.2015	Teva Pharmaceutical Works Private Limited Company	(J05AR01) Zidovudine and Lamivudine
43	№ RK-LS-5№019229	**Mivux**	Registration	14.05.2015	NOBEL ALMATY PHARMACEUTICAL FACTORY	(J05AF05) Lamivudine
44	RK-LS-5№016643	**Nevipan**	Re-registration	14.07.2016	Ranbaxy Laboratories Limited	(J05AG01) Nevirapine
45	№ RK-LS-5№013327	**Nevir™**	Registration	12.12.2014	Emcure Pharmaceuticals Ltd.	(J05AG01) Nevirapine
46	№ RK-LS-5№023603	**Nevirapine**	Registration	09.04.2018	Macleods Pharmaceuticals Ltd	(J05AG01) Nevirapine
47	RK-LS-5№022943	**Nevirapine**	Registration	27.04.2017	Strides Shasun Limited	(J05AG01) Nevirapine
48	RK-LS-5№021443	**Nevirapine**	Registration	25.06.2015	Aurobindo Pharma Limited	(J05AG01) Nevirapine
49	RK-LS-5№020782	**Nevirapine**	Registration	09.09.2014	Aurobindo Pharma Limited	(J05AG01) Nevirapine
50	RK-LS-5№020659	**Nevirapine**	Registration	18.06.2014	Mylan Laboratories Limited	(J05AG01) Nevirapine
51	№ RK-LS-5№021797	**Nevirpine**	Registration	06.11.2015	JSC “Pharmasyntez”	(J05AG01) Nevirapine
52	RK-LS-5№017855	**Norvir**	Re-registration	21.02.2017	AbbVie Deutschland GmbH & Co. KГ	(J05AE03) Ritonavir
53	RK-LS-5№121662	**Olitide**	Registration	14.10.2015	JSC “Pharmasyntez”	(J05AF06) Abacavir
54	RK-LS-5№121663	**Olitide**	Registration	14.10.2015	JSC “Pharmasyntez”	(J05AF06) Abacavir
55	RK-LS-5№021033	**Prezista**	Registration	08.12.2014	Janssen-Orto LLC	(J05AE10) Darunavir
56	RK-LS-5№019606	**Prezista**	Registration	14.11.2017	Janssen-Orto LLC	(J05AE10) Darunavir
57	RK-LS-5№019607	**Prezista**	Registration	14.11.2017	Janssen-Orto LLC	(J05AE10) Darunavir
58	RK-LS-5№121728	**Regast**	Registration	19.10.2015	JSC “Pharmasyntez”	(J05AG03) Efavirenz
59	RK-LS-5№121729	**Regast**	Registration	19.10.2015	JSC “Pharmasyntez”	(J05AG03) Efavirenz
60	RK-LS-5№022425	**Rezolsta**	Registration	13.10.2016	Janssen-Orto LLC	(J05AR14) Darunavir, Cobicistat
61	RK-LS-5№011013	**Retrovir**	Re-registration	13.04.2018	GlaxoSmithKline Inc.	(J05AF01) Zidovudine
62	RK-LS-5№011012	**Retrovir**	Re-registration	06.06.2018	GlaxoSmithKline Pharmaceuticals Ltd.	(J05AF01) Zidovudine

63	RK-LS-5№018110	**Stokrin**	Re-registration	30.06.2016	Zhejiang Huahai Pharmaceutical Co., Ltd.	(J05AG03) Efavirenz
64	№ RK-LS-5 №020692	**Tavin**	Registration	02.07.2014	Emcure Pharmaceuticals Ltd	(J05AF07) Tenofovir disoproxil
65	RK-LS-5№019269	**Telzir**	Re-registration	07.09.2017	Glaxo Operations UK ltd, Glaxo Wellcome Opeations	(J05AE07) Fosamprenavir
66	RK-LS-5№018506	**Telzir**	Re-registration	03.05.2017	GlaxoSmithKline Inc.	(J05AE07) Fosamprenavir
67	RK-LS-5№020718	**Tenofovir disoproxil Fumarate**	Registration	23.07.2014	Aurobindo Pharma Limited	(J05AF07) Tenofovir a disoproxil
68	RK-LS-5№020658	**Tenofovir disoproxil Fumarate**	Registration	18.06.2014	Mylan Laboratories Limited	(J05AF07) Tenofovir a disoproxil
69	RK-LS-5№020764	**Tenofovir disoproxil Fumarate and Lamivudine**	Registration	02.09.2014	Mylan Laboratories Limited	(J05AR) Antiviral drugs active against HIV, combinations
70	RK-LS-5№020654	**Tenofovir disoproxil Fumarate and Emtricitabine**	Registration	18.06.2014	Mylan Laboratories Limited	(J05AR03) Tenofovir disoproxil and Emtricitabine
71	RK-LS-5№020763	**Tenofovir disoproxil Fumarate, Lamivudine and Efavirenz**	Registration	02.09.2014	Mylan Laboratories Limited	(J05AR11) Lamivudine, Tenofovir a disoproxil and Efavirenz
72	RK-LS-5№020764	**Tenofovir disoproxil Fumarate, Lamivudine and Efavirenz**	Registration	02.09.2014	Mylan Laboratories Limited	(J05AR11) Lamivudine, Tenofovir a disoproxil and Efavirenz
73	RK-LS-5№020655	**Tenofovir disoproxil Fumarate, Emtricitabine and Efavirenz**	Registration	18.06.2014	Mylan Laboratories Limited	(J05AR06) Emtricitabine, Tenofovir Disoproxil and Efavirenz
74	RK-LS-5№021169	**Tivicay**	Registration	04.02.2015	Glaxo Operations UK ltd, Glaxo Wellcome Opeations	(J05AX12) Dolutegravir
75	RK-LS-5№012399	**Trizivir**	Re-registration	01.11.2018	GlaxoSmithKline Pharmaceuticals Ltd.	(J05AR04) Zidovudine, Lamivudine and Abacavir
76	RK-LS-5№022415	**Triumeq**	Registration	10.10.2016	Glaxo Operations UK ltd, Glaxo Wellcome Opeations	(J05AR13) Lamivudine, Abacavir and Dolutegravir
77	RK-LS-5№020832	**Truvada**	Registration	07.10.2014	Takeda GmbH	(J05AR03) Tenofovir disoproxil and Emtricitabine
78	RK-LS-5№022471	**Edurant**	Registration	15.11.2016	Janssen-Cilag Inc.	(J05AG05) Rilpivirine

79	№ RK-LS-5№020612	**Emtriten**	Registration	03.06.2014	Hetero Labs Limited for NV Holding, Hong Kong	(J05AR03)Tenofovir a disoproxil and Emtricitabine
80	№ RK-LS-5№023521	**Emtricitabine/ Tenofovir**	Registration	09.02.2018	Strides Shasun Limited	(J05AF) Nucleosides - reverse transcriptase inhibitors
81	№ RK-LS-5№023559	**Emtricitabine/ Tenofovir - КРКА**	Registration	02.03.2018	Krka, d. d	(J05AR03) Tenofovir a disoproxil and Emtricitabine
82	RK-LS-5№015500	**Epivir**	Re-registration	19.11.2014	GlaxoSmithKline Pharmaceuticals Ltd.	(J05AF05) Lamivudine
83	№ RK-LS-5№021044	**Этенем**	Registration	08.12.2014	Hetero Labs Limited for NV Holding, Hong Kong	(J05AR06) Emtricitabine, Tenofovir Disoproxil and Efavirenz
84	№ RK-LS-5№023633	**Efavirenz**	Registration	04.05.2018	Macleods Pharmaceuticals Ltd	(J05AG03) Efavirenz
85	RK-LS-5№020725	**Efavirenz, Emtricitabine and Tenofovir disoproxil Fumarate**	Registration	23.07.2014	Aurobindo Pharma Limited	(J05AR06) Emtricitabine, Tenofovir Disoproxil and Efavirenz
86	№ RK-LS-5№023679	**Efavirenz/Emtricitabine/Tenofovir**	Registration	31.05.2018	Strides Shasun Limited	(J05AR06) Emtricitabine, Tenofovir disoproxil and Efavirenz
87	№ RK-LS-5№121729	**Efavirenz-AIGF**	Registration	19.10.2015	Abdi Ibrahim Global Pharm	(J05AG03) Efavirenz
88	№ RK-LS-5№121728	**Efavirenz-AIGF**	Registration	19.10.2015	Abdi Ibrahim Global Pharm	(J05AG03) Efavirenz
89	RK-LS-5№020848	**Efavirenz-Тева**	Registration	07.10.2014	Pliva Croatia Ltd	(J05AG03) Efavirenz
90	№ RK-LS-5№005492	**Eferven**	Re-registration	29.12.2017	Sun Pharmaceutical Industries Limited	(J05AG03) Efavirenz

Annex 2

Table 2. ARV drugs purchased by the Sole Distributor in 2018.

INN	Drug dosage form	Brand Name	Pre-packing	Quantity, unit	Number of Packs	Supplier
Zidovudine + Lamivudine	Coated tablets, 300 mg/ 150 mg	Duolazide	60	1693440	28224	Abdi Ibrahim Global Pharm, LLP
Dolutegravir	Film-coated tablets, 50 mg	Tivicay	30	404250	13475	GSK Kazakhstan, LLP
Abacavir+ Lamivudine	Film-coated tablets	Kivexa	30	561780	18726	UNICEF, United Nations Children's Fund
Lopinavir + Ritonavir	Film-coated tablets 200 mg/50 mg	Aluvia	120	2022600	16855	VIVA PHARM, LTD
Darunavir	Film-coated tablets, 800 mg, 1 tablet of Norvir 100 mg with each unit of the drug	Prezista	30	113970	3799	UNICEF, United Nations Children's Fund
Abacavir+Lamivudine+Zidovudine	Film-coated tablets 300mg/150mg/300mg	Trizivir	60	209160	3486	GSK Kazakhstan, LLP
Darunavir	Film-coated tablets, 600mg, 1 tablet Norvira 100 mg with each unit of the drug	Prezista	60	97140	1619	UNICEF, United Nations Children's Fund
Tenofovir+Emtricitabine+Efavirenz	Film-coated tablets, 300 mg/200 mg/600 mg	Tenofovira Disoproxil Fumarate, Emtricitabine and Efavirenz	30	2703420	90114	UNICEF, United Nations Children's Fund
Etravirine	Tablets 200 mg	Intelens	60	95460	1591	Janssen Pharmaceutica
Darunavir	Film-coated tablets 400 mg, 1 tablet Norvira 100 mg with each unit of the drug (INN – Ritonavir)	Prezista	60	94740	1579	UNICEF, United Nations Children's Fund
Lopinavir + Ritonavir	Film-coated tablets 200 mg/50 mg	Aluvia	120	654360	5453	VIVA PHARM, LTD
Etravirine	Tablets 100 mg	Intelens	120	124080	1034	Janssen Pharmaceutica
Dolutegravir	Film-coated tablets, 50 mg	Tivicay	30	31980	1066	GSK Kazakhstan, LLP
Abacavir	Coated tablets, 300 mg	Virakar	60	89340	1489	Abdi Ibrahim Global Pharm, LLP
Emtricitabine+Tenofovir	Tablets, 300 mg/200 mg	Tenofovira Disoproxil Fumarate and Emtricitabine	30	901440	30048	UNICEF, United Nations Children's Fund

INN	Drug dosage form	Brand Name	Pre-packing	Quantity, unit	Number of Packs	Supplier
Abacavir+Lamivudine	Film-coated tablets	Kivexa	30	27990	933	INKAR, LLP
Tenofovir	Film-coated tablets, 300 mg	Tenofovir Disoproxil Fumarate	30	772710	25757	UNICEF, United Nations Children's Fund
Zidovudine	Oral solution, 10 mg/ml, 200 ml	Retrovir	1	3225	3225	GSK Kazakhstan, LLP
Zidovudine+ Lamivudine	Coated tablets, 300 mg/150 mg	Combivir	60	111060	1851	INKAR, LLP
Abacavir+ Lamivudine	Film-coated tablets	Kivexa	30	15240	508	INKAR, LLP
Efavirenz	Tablets, 600 mg	Efavirenz (Efavirenz)	30	644370	21479	UNICEF, United Nations Children's Fund
Efavirenz	Coated tablets, 200mg	Stokrin	90	69300	770	AK NIET, LTD
Lopinavir + Ritonavir	Film-coated tablets, 200 mg/50 mg	Aluvia	120	76920	641	VIVA PHARM, LTD
Abacavir	Film-coated tablets, 300 mg	Ziagen	60	28560	476	INKAR, LLP
Zidovudine+ Lamivudine	Coated tablets	Combivir	60	63480	1058	INKAR, LLP
Abacavir	Oral solution, 20 mg/ml, 240 ml	Ziagen	1	524	524	GSK Kazakhstan, LLP
Abacavir	Film-coated tablets, 300 mg	Ziagen	60	23460	391	INKAR, LLP
Etravirine	Tablets 200 mg	Intelens	60	6300	105	Janssen Pharmaceutica
Nevirapine	Tablets, 200 mg	Nevirapine (Nevirapine)	60	605460	10091	UNICEF, United Nations Children's Fund
Nevirapine	Tablets, 200 mg	Viramune	60	39960	666	Kazakh pharmaceutical company «MEDSERVICE PLUS», LLP
Lopinavir + Ritonavir	Film-coated tablets, 200 mg/50 mg	Aluvia	120	29760	248	VIVA PHARM, LTD
Lopinavir + Ritonavir	Film-coated tablets, 100 mg/25 mg	Aluvia	60	84540	1409	VIVA PHARM, LTD
Zidovudine	Capsules 100 mg	Retrovir	100	35500	355	INKAR, LLP

INN	Drug dosage form	Brand Name	Pre-packing	Quantity, unit	Number of Packs	Supplier
Nevirapine	Tablets 200 mg	Viramune	60	19200	320	Kazakh pharmaceutical company «MEDSERVICE PLUS», LLP
Lopinavir + Ritonavir	Oral solution, 60 ml	Kaletra	5	770	154	VIVA PHARM, LTD
Zidovudine	Capsules, 100 mg	Zidoas	100	20800	208	Abdi Ibrahim Global Pharm, LLP
Efavirenz	Tablets, 200 mg	Efavirenz (Efavirenz)	90	55710	619	UNICEF, United Nations Children's Fund
Lopinavir + Ritonavir	Tablets, ппо100 mg/25 mg	Aluvia	60	31380	523	VIVA PHARM, LTD
Emtricitabine+ Tenofovir	Film-coated tablets	Truvada	30	2910	97	UNICEF, United Nations Children's Fund
Zidovudine	Capsules 100 mg	Retrovir	100	16400	164	INKAR, LLP
Lopinavir + Ritonavir	Oral solution 60 ml	Kaletra	5	335	67	VIVA PHARM, LTD
Zidovudine	Tablets, 300 mg	Zidovudine (Zidovudine)	60	9420	157	UNICEF, United Nations Children's Fund

Annex 3.

Table 3. Cost of each drug in total budget

INN	Brand Name	Manufacturer	Number of units	Supplier's cost, KZT	Supplier's cost, USD [101]	Share of total budget for ARV drugs, %
Abacavir, 300mg	Virakar	Abdi Ibrahim Global Pharm, LLP	89340	52 119 163,20	138 947,38	1,08
Abacavir, 300 mg	Ziagen	INKAR, LLP	28560	13 308 960,00	35 481,10	0,28
Abacavir, 20 mg/ ml, 240 ml	Ziagen	GSK Kazakhstan, LLP	524	11 318 400,00	30 174,35	0,23
Abacavir, 300mg	Ziagen	INKAR, LLP	23460	10 932 360,00	29 145,19	0,23
Abacavir+ Lamivudine	Kivexa	UNICEF, United Nations Children's Fund	561780	463 633 219,51	1 236 025,65	9,61
Abacavir+ Lamivudine	Kivexa	INKAR, LLP	27990	34 707 600,00	92 528,93	0,72
Abacavir+ Lamivudine	Kivexa	INKAR, LLP	15240	18 897 600,00	50 380,17	0,39
Abacavir+ Lamivudine+ Zidovudine, 300mg/150mg/300mg	Trizivir	GSK Kazakhstan, LLP	209160	252 820 058,40	674 007,09	5,24
Darunavir, 800 mg, 1 tablet Norvir 100 mg with each unit of the drug	Prezista	UNICEF, United Nations Children's Fund	113970	329 725 970,19	879 034,84	6,84
Darunavir, 600mg, 1 tablet Norvir 100 mg with each unit of the drug	Prezista	UNICEF, United Nations Children's Fund	97140	208 102 677,97	554 792,53	4,31
Darunavir, 400 mg, 1 tablet Norvir 100 mg with each 2 units of the drug	Prezista	UNICEF, United Nations Children's Fund	94740	137 013 592,96	365 272,18	2,84
Dolutegravir, 50 mg	Tivicay	GSK Kazakhstan, LLP	404250	834 803 201,35	2 225 548,39	17,31
Dolutegravir, 50 mg	Tivicay	GSK Kazakhstan, LLP	31980	66 040 832,11	176 061,94	1,37
Zidovudine, 10 mg/ml, 200 ml	Retrovir	GSK Kazakhstan, LLP	3225	22 245 050,25	59 304,32	0,46
Zidovudine, 100 mg	Retrovir	INKAR, LLP	35500	3 550 000,00	9 464,14	0,07
Zidovudine, 100mg	Zidoas	Abdi Ibrahim Global Pharm, LLP	20800	2 207 920,00	5 886,22	0,05
Zidovudine, 100mg	Retrovir	INKAR, LLP	16400	1 649 840,00	4 398,40	0,03
Zidovudine, 300mg	Zidovudine (Zidovudine)	UNICEF, United Nations Children's Fund	9420	211 183,62	563,01	0,0044
Zidovudine+ Lamivudine, 300 mg/150 mg	Duolazide	Abdi Ibrahim Global Pharm, LLP	1693440	1 279 749 542,40	3 411 755,64	**26,53**
Zidovudine+ Lamivudine, 300 mg/150 mg	Combivir	INKAR, LLP	111060	21 812 184,00	58 150,32	0,45
Zidovudine+ Lamivudine	Combivir	INKAR, LLP	63480	12 467 472,00	33 237,73	0,26
Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	VIVA PHARM, LTD	2022600	351 467 202,00	936 996,01	**7,29**
Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	VIVA PHARM, LTD	654360	113 708 137,20	303 140,86	2,36
Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	VIVA PHARM, LTD	76920	13 366 388,40	35 634,20	0,28
Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	VIVA PHARM, LTD	29760	5 171 395,20	13 786,71	0,11

[101] Dollar exchange rate on 01.01.2019 = 375.10 tenge

INN	Brand Name	Manufacturer	Number of units	Supplier's cost, KZT	Supplier's cost, USD [101]	Share of total budget for ARV drugs, %
Lopinavir + Ritonavir, 100 mg/25 mg	Aluvia	VIVA PHARM, LTD	84540	5 053 801,20	13 473,21	0,10
Lopinavir+ Ritonavir, 6 ml	Kaletra	VIVA PHARM, LTD	770	2 460 234,70	6 558,88	0,05
Lopinavir+ Ritonavir, 100 mg/25 mg	Aluvia	VIVA PHARM, LTD	31380	1 875 896,40	5 001,06	0,04
Lopinavir+ Ritonavir, 60 ml	Kaletra	VIVA PHARM, LTD	335	1 070 361,85	2 853,54	0,02
Nevirapine, 200 mg	Nevirapine (Nevirapine)	UNICEF, United Nations Children's Fund	605460	6 686 498,42	17 825,91	0,14
Nevirapine, 200 mg	Viramune	Kazakh pharmaceutical company «MEDSERVICE PLUS», LLP	39960	5 714 280,00	15 234,02	0,12
Nevirapine, 200mg	Viramune	Kazakh pharmaceutical company «MEDSERVICE PLUS», LLP	19200	2 764 800,00	7 370,83	0,06
Tenofovir, 300mg	Tenofovir Disoproxil Fumarate	UNICEF, United Nations Children's Fund	772710	29 867 430,84	79 625,25	0,62
Tenofovir+ Emtricitabine+ Efavirenz, 300 mg/200 mg/600 mg	Tenofovir Disoproxil Fumarate, Emtricitabine and Efavirenz	UNICEF, United Nations Children's Fund	2703420	186 597 933,37	497 461,83	3,87
Emtricitabine+ Tenofovir, 300 mg/200 mg	Tenofovir disoproxil Fumarate and Emtricitabine	UNICEF, United Nations Children's Fund	901440	38 924 843,26	103 771,91	0,81
Emtricitabine+ Tenofovir	Truvada	UNICEF, United Nations Children's Fund	2910	1 698 122,78	4 527,12	0,04
Etravirine, 200 mg	Intelens	Janssen Pharmaceutica	95460	142 703 444,30	380 441,07	2,96
Etravirine, 100 mg	Intelens	Janssen Pharmaceutica	124080	92 743 788,19	247 250,83	1,92
Etravirine, 200 mg	Intelens	Janssen Pharmaceutica	6300	9 417 889,16	25 107,68	0,20
Efavirenz, 600mg	Efavirenz (Efavirenz)	UNICEF, United Nations Children's Fund	644370	17 007 735,89	45 341,87	0,35
Efavirenz, 200 mg	Stokrin	AK NIET, LTD	69300	15 355 494,00	40 937,07	0,32
Efavirenz, 200 mg	Efavirenz (Efavirenz)	UNICEF, United Nations Children's Fund	55710	1 907 252,28	5 084,65	0,04
TOTAL				**4 822 879 757,40**	**12 857 584,00**	

Annex 4

Table 4. Actual prices and contract amounts for ARV drugs purchased in 2018.

INN	Brand Name	Drug dosage form	Manufacturer	Supplier's cost per unit, KZT	Supplier's cost per package, KZT	Cost per patient per year, KZT	Cost per patient per year, USD[102]	Total amount, Supplier's price
Abacavir, 300mg	Virakar	60	Abdi Ibrahim Global Pharm, LLP, Kazakhstan	583,38	35 002,80	425 867,40	1 135,34	52 119 163,20
Abacavir, 300 mg	Ziagen	60	GlaxoSmithKline Pharmaceuticals Ltd.,	466,00	27 960,00	340 180,00	906,90	13 308 960,00
Abacavir, 20 mg/ml, 240 ml	Ziagen	1	GlaxoSmithKline Inc., Canada	21 600,00	21 600,00	0,00	0,00	11 318 400,00
Abacavir, 300mg	Ziagen	60	GlaxoSmithKline Pharmaceuticals Ltd.,	466,00	27 960,00	340 180,00	906,90	10 932 360,00
Abacavir+ Lamivudine	Kivexa	30	GlaxoSmithKline Pharmaceuticals Ltd.,	825,29	24 758,80	301 232,02	803,07	463 633 219,51
Abacavir+ Lamivudine	Kivexa	30	Glaxo Operations, United Kingdom, LLP.	1 240,00	37 200,00	452 600,00	1 206,61	34 707 600,00
Abacavir+ Lamivudine	Kivexa	30	Glaxo Operations, United Kingdom, LLP.	1 240,00	37 200,00	452 600,00	1 206,61	18 897 600,00
Abacavir+ Lamivudine+ Zidovudine, 300mg/150mg/300mg	Trizivir	60	GlaxoSmithKline Pharmaceuticals Ltd., Poland,	1 208,74	72 524,40	882 380,20	2 352,39	252 820 058,40
Darunavir, 800 mg, с каждой 1 tablet Norvir 100 mg with each unit of the drug	Prezista	30	Janssen-Orto LLC, Puerto-Rico,	2 893,09	86 792,83	1 055 979,46	2 815,19	329 725 970,19
Darunavir, 600mg, 1 tablet Norvir 100 mg with each unit of the drug	Prezista	60	Janssen-Orto LLC, Puerto-Rico,	2 142,30	128 537,79	1 563 876,41	4 169,23	208 102 677,97
Darunavir, 400 mg, 1 tablet Norvir 100 mg with each 2 units of the drug (INN – Ritonavir)	Prezista	60	Janssen-Orto LLC, Puerto-Rico,	1 446,21	86 772,38	1 055 730,66	2 814,53	137 013 592,96
Dolutegravir, 50 mg	Tivicay	30	Glaxo Operations, United Kingdom Limited	2 065,07	61 952,00	753 749,33	2 009,46	834 803 201,35
Dolutegravir, 50 mg	Tivicay	30	Glaxo Operations, United Kingdom Limited	2 065,07	61 952,00	753 749,33	2 009,46	66 040 832,11
Zidovudine, 10 mg/ml, 200 ml	Retrovir	1	GlaxoSmithKline Inc., Canada,	6 897,69	6 897,69	0,00	0,00	22 245 050,25
Zidovudine, 100 mg	Retrovir	100	GlaxoSmithKline	100,00	10 000,00	219 000,00	583,84	3 550 000,00
Zidovudine, 100mg	Zidoas	100	Abdi Ibrahim Global Pharm, LLP, Kazakhstan	106,15	10 615,00	232 468,50	619,75	2 207 920,00
Zidovudine, 100mg	Retrovir	100	GlaxoSmithKline Pharmaceuticals Ltd.,	100,60	10 060,00	220 314,00	587,35	1 649 840,00

[102]Children's forms were not calculated, since the dosage depends on the child's age.

INN	Brand Name	Drug dosage form	Manufacturer	Supplier's cost per unit, KZT	Supplier's cost per package, KZT	Cost per patient per year, KZT	Cost per patient per year, USD[102]	Total amount, Supplier's price
Zidovudine, 300mg	Zidovudine (Zidovudine)	60	Micro Labs, India	22,42	1 345,12	16 365,61	43,63	211 183,62
Zidovudine+ Lamivudine, 300 mg/150 mg	Duolazide	60	Abdi Ibrahim Global Pharm, LLP, Kazakhstan	755,71	45 342,60	551 668,30	1 470,72	1 279 749 542,40
Zidovudine+ Lamivudine, 300 mg/150 mg	Combivir	60	GlaxoSmithKline Pharmaceuticals Ltd.,	196,40	11 784,00	143 372,00	382,22	21 812 184,00
Zidovudine+ Lamivudine	Combivir	60	GlaxoSmithKline Pharmaceuticals Ltd.,	196,40	11 784,00	143 372,00	382,22	12 467 472,00
Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	120	AbbVie Deutschland GmbH & Co., Germany,	173,77	20 852,40	253 704,20	676,36	351 467 202,00
Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	120	AbbVie Deutschland GmbH & Co., Germany,	173,77	20 852,40	253 704,20	676,36	113 708 137,20
Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	120	AbbVie Deutschland GmbH & Co.	173,77	20 852,40	253 704,20	676,36	13 366 388,40
Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	120	AbbVie Deutschland GmbH & Co., Germany,	173,77	20 852,40	253 704,20	676,36	5 171 395,20
Lopinavir + Ritonavir, 100 mg/25 mg	Aluvia	60	AbbVie Deutschland GmbH & Co,	59,78	3 586,80	0,00	0,00	5 053 801,20
Lopinavir+ Ritonavir, 6 ml	Kaletra	5	Aesica Queenborough Ltd., United Kingdom, owner of the Abbwee	3 195,11	15 975,55	0,00	0,00	2 460 234,70
Lopinavir+ Ritonavir, 100 mg/25 mg	Aluvia	60	AbbVie Deutschland GmbH & Co, Germany,	59,78	3 586,80	0,00	0,00	1 875 896,40
Lopinavir+ Ritonavir, 60 ml	Kaletra	5	Aesica Queenborough Ltd., United Kingdom, owner of the Abbwee	3 195,11	15 975,55	0,00	0,00	1 070 361,85
Nevirapine, 200 mg	Nevirapine (Nevirapine)	60	Mylan Laboratories Limited, India	11,04	662,62	8 061,88	21,49	6 686 498,42
Nevirapine, 200 mg	Viramune	60	Boehringer Ingelheim GmbH,	143,00	8 580,00	104 390,00	278,30	5 714 280,00
Nevirapine, 200mg	Viramune	60	Boehringer Ingelheim GmbH,	144,00	8 640,00	105 120,00	280,25	2 764 800,00
Tenofovir, 300mg	Tenofovir Disoproxil Fumarate	30	Mylan Laboratories Limited, India	38,65	1 159,58	14 108,28	37,61	29 867 430,84

INN	Brand Name	Drug dosage form	Manufacturer	Supplier's cost per unit, KZT	Supplier's cost per package, KZT	Cost per patient per year, KZT	Cost per patient per year, USD[102]	Total amount, Supplier's price
Tenofovir+ Emtricitabine+Efavirenz, 300 mg/200 mg/600 mg	Tenofovir Disoproxil Fumarate Emtricitabine and Efavirenz	30	Mylan Laboratories Limited, India	69,02	2 070,69	25 193,36	67,16	186 597 933,37
Emtricitabine+ Tenofovir, 300 mg/200 mg	Tenofovir disoproxil Fumarate and Emtricitabine	30	Micro Labs, India	43,18	1 295,42	15 760,97	42,02	38 924 843,26
Emtricitabine+ Tenofovir	Truvada	30	Takeda GmbH, Germany, owner Gilead Sciences,	583,55	17 506,42	212 994,78	567,83	1 698 122,78
Etravirine, 200 mg	Intelens	60	Janssen-Cilag Inc., Italy, owner of LLC Johnson & Johnson, RUSSIA	1 494,90	89 694,18	1 091 279,22	2 909,30	142 703 444,30
Etravirine, 100 mg	Intelens	120	Janssen-Cilag Inc., Italy,	747,45	89 694,19	1 091 279,26	2 909,30	92 743 788,19
Etravirine, 200 mg	Intelens	60	Janssen-Cilag Inc.,	1 494,90	89 694,18	1 091 279,22	2 909,30	9 417 889,16
Efavirenz, 600mg	Efavirenz (Efavirenz)	30	Hetero Labs Limited, India	26,39	791,83	9 633,94	25,68	17 007 735,89
Efavirenz, 200 mg	Stokrin	90	Zhejiang Huahai Pharmaceutical Co., Ltd, China	221,58	19 942,20	242 630,10	646,84	15 355 494,00
Efavirenz, 200 mg	Efavirenz (Efavirenz)	90	Strides Shasun Limited, India	34,24	3 081,18	37 487,73	99,94	1 907 252,28
TOTAL								**4,822,879,757.40**

Annex 5

Table 7. Estimated number of annual regimens foreach ARV drug

No	INN	Brand Name	Drug dosage form	Manufacturer	Dosing schedule (number of tablets per day)	Number of units	Estimated number of annual treatment courses	Category of patients [103]
1	Abacavir, 300mg	Virakar	60	Abdi Ibrahim Global Pharm, LLP, Kazakhstan	2	89340	122,38	Adults
2	Abacavir, 300 mg	Ziagen	60	GlaxoSmithKline Pharmaceuticals Ltd.,	2	28560	0,00	Children
3	Abacavir, 20 mg/ ml, 240 ml	Ziagen	1	GlaxoSmithKline Inc., Canada,	0	524	0,00	Children
4	Abacavir, 300mg	Ziagen	60	GlaxoSmithKline Pharmaceuticals Ltd.	2	23460	32,14	Adults
5	Abacavir+ Lamivudine	Kivexa	30	GlaxoSmithKline Pharmaceuticals Ltd.	1	561780	1 539,12	Adults
6	Abacavir+ Lamivudine	Kivexa	30	Glaxo Operations United Kingdom Ltd.	1	27990	0,00	Children
7	Abacavir+ Lamivudine	Kivexa	30	Glaxo Operations United Kingdom Ltd.	1	15240	41,75	Adults
8	Abacavir+ Lamivudine+ Zidovudine, 300mg/150mg/300mg	Trizivir	60	GlaxoSmithKline Pharmaceuticals Ltd., Poland,	2	209160	286,52	Adults
9	Darunavir, 800 mg, 1 tablet Norvir 100 mg with each unit of the drug	Prezista	30	Janssen-Orto LLC, Puerto-Rico,	1	113970	312,25	Adults
10	Darunavir, 600mg, 1 tablet Norvir 100 mg with each unit of the drug	Prezista	60	Janssen-Orto LLC, Puerto-Rico,	2	97140	133,07	Adults
11	Darunavir, 400 mg, 1 tablet Norvir 100 mg with each unit of the drug	Prezista	60	Janssen-Orto LLC, Puerto-Rico,	2	94740	129,78	Adults
12	Dolutegravir, 50 mg	Tivicay	30	Glaxo Operations, United Kingdom Limited	1	404250	1 107,53	Adults
13	Dolutegravir, 50 mg	Tivicay	30	Glaxo Operations, United Kingdom Limited	1	31980	87,62	Adults
14	Zidovudine, 10 mg/ ml, 200 ml	Retrovir	1	GlaxoSmithKline Inc., Canada,	0	3225	0,00	Children
15	Zidovudine, 100 mg	Retrovir	100	GlaxoSmithKline	6	35500	0,00	Children
16	Zidovudine, 100mg	Zidoas	100	Abdi Ibrahim Global Pharm, LLP, Kazakhstan	6	20800	9,50	Adults
17	Zidovudine, 100mg	Retrovir	100	GlaxoSmithKline Pharmaceuticals Ltd.	6	16400	0,00	Children
18	Zidovudine, 300mg	Zidovudine (Zidovudine)	60	Micro Labs, India	2	9420	12,90	Adults
19	Zidovudine+ Lamivudine, 300 mg/150 mg	Duolazide	60	Abdi Ibrahim Global Pharm, LLP, Kazakhstan	2	1693440	2 319,78	Adults
20	Zidovudine+ Lamivudine, 300 mg/150 mg	Combivir	60	GlaxoSmithKline Pharmaceuticals Ltd.	2	111060	0,00	Children

[102] Children's forms were not calculated, since the dosage depends on the child's age

No	INN	Brand Name	Drug dosage form	Manufacturer	Dosing schedule (number of tablets per day)	Number of units	Estimated number of annual treatment courses	Category of patients [99]
21	Zidovudine+ Lamivudine	Combivir	60	GlaxoSmithKline Pharmaceuticals Ltd.	2	63480	0,00	Children
22	Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	120	AbbVie Deutschland GmbH & Co. KГ, Germany,	4	2022600	1 385,34	Adults
23	Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	120	AbbVie Deutschland GmbH & Co, Germany,	4	654360	448,19	Adults
24	Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	120	AbbVie Deutschland GmbH & Co.	4	76920	52,68	Adults
25	Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	120	AbbVie Deutschland GmbH & Co., Germany,	4	29760	20,38	Adults
26	Lopinavir + Ritonavir, 100 mg/25 mg	Aluvia	60	AbbVie Deutschland GmbH & Co,	0	84540	0,00	Children
27	Lopinavir+ Ritonavir, 6 ml	Kaletra	5	Aesica Queenborough Ltd., United Kingdom, owner of Abbwee RU	0	770	0,00	Children
28	Lopinavir+ Ritonavir, 100 mg/25 mg	Aluvia	60	AbbVie Deutschland GmbH & Co, Germany,	0	31380	0,00	Children
29	Lopinavir+ Ritonavir, 60 ml	Kaletra	5	Aesica Queenborough Ltd., United Kingdom, owner of Abbwee RU	0	335	0,00	Children
30	Nevirapine, 200 mg	Nevirapine (Nevirapine)	60	Mylan Laboratories Limited, India	2	605460	829,40	Adults
31	Nevirapine, 200 mg	Viramune	60	Boehringer Ingelheim GmbH,	2	39960	0,00	Children
32	Nevirapine, 200mg	Viramune	60	Boehringer Ingelheim GmbH	2	19200	0,00	Children
33	Tenofovir, 300mg	Tenofovir Disoproxil Fumarate	30	Mylan Laboratories Limited, India	1	772710	2 117,01	Adults
34	Tenofovir+ Emtricitabine+Efavirenz, 300 mg/200 mg/600 mg	Tenofovir disoproxil Fumarate, Emtricitabine and Efavirenz	30	Mylan Laboratories Limited, India	1	2703420	7 406,63	Adults
35	Emtricitabine+ Tenofovir, 300 mg/200 mg	Tenofovir Disoproxil Fumarate and Emtricitabine	30	Micro Labs, India	1	901440	2 469,70	Adults
36	Emtricitabine+ Tenofovir	Truvada	30	Takeda GmbH, Germany, owner Gilead Sciences, RU	1	2910	0,00	Children
37	Etravirine, 200 mg	Intelens	60	Janssen-Cilag Inc., Italy, owner of LLC Johnson & Johnson, RUSSIA	2	95460	130,77	Adults
38	Etravirine, 100 mg	Intelens	120	Janssen-Cilag Inc., Italy,	4	124080	84,99	Adults
39	Etravirine, 200 mg	Intelens	60	Janssen-Cilag Inc.,	2	6300	8,63	Adults
40	Efavirenz, 600mg	Efavirenz (Efavirenz)	30	Hetero Labs Limited, India	1	644370	1 765,40	Adults

No	INN	Brand Name	Drug dosage form	Manufacturer	Dosing schedule (number of tablets per day)	Number of units	Estimated number of annual treatment courses	Category of patients [99]
41	Efavirenz, 200 mg	Stokrin	90	Zhejiang Huahai Pharmaceutical Co., Ltd, China	3	69300	0,00	Children
42	Efavirenz, 200 mg	Efavirenz (Efavirenz)	90	Strides Shasun Limited India	3	55710	50,88	Adults

Annex 6

Table 6. List of registered medicines to treat HCV in Kazakhstan

No	Product licence number	International non-proprietory name (INN)	Brand name	Type of action	Marketing start date (dd/mm/yy)	Manufacturer	Price (KZT)	ATC-code
1	RK-LS-5№012328	Pegylated interferon alpha-2a	PEGASIS	Re-registration	26.12.2018	F. Hoffmann-La Roche Ltd	56 966,31	L03AB11
2	RK-LS -5№020479 on RK-LS - 5№020484	Cepeginterferon alfa-2b	ALGERON	Registration	11.04.2014	BIOCAD		L03AB14
3	RK-LS - 5№022268/69	Pegylated interferon alpha-2b	Pegaltivir	Registration	14.07.2016	OJSC Pharmstandard -Ufa VITA		L03AB10
4	RK-LS -5№023266	Elbasvir / Grazoprevir	ZEPATIER	Registration	27.09.2017	MSD		J05AX68
5	RK-LS -5№023818	Glecaprevir / Pibrentasvir	MAVYRET	Registration	10.09.2018	AbbVie		J05AX
6	RK-LS -5№021846	Dasabuvir/ Ombitasvir / Paritaprevir / Ritonavir	VIEKIRA PAK	Registration	25.11.2015	AbbVie	35 524,88[103]	J05AP52
7	RK-LS- 5№022460	Sofosbuvir / Ledipasvir	HARVONI	Registration	02.11.2016	Patheon Inc.	78 181,70	J05AP51
8	RK-LS -5№000663	Ribavirin	COPEGUS	Registration	12.04.2016	F. Hoffmann-La Roche Ltd	36, 90	J05AB04
9	RK-LS -5№017878	Ribavirin	RIVIRIN	Re-registration	03.06.2014	Abdi İbrahim Global Pharm	36,90	J05AB04
10	RK-LS 5№005086	Ribavirin	REBETOL	Re-registration	21.02.2017	MSD International GmbH (Puerto Rico Branch) LLC	32 134 ,33	J05AB04
11	RK-LS 5№022490	Sofosbuvir	SOFGEN	Registration	24.11.2016	Hetero Labs Limited.	4. .424. 00*	J05AX15
12	RK-LS 5№023213	Sofosbuvir	VIRSO	Registration	07.09.2017	Strides Shasun Limited		J05AX15
13	RK-LS 5№022703	Sofosbuvir	GRATEZIANO	Registration	20.01.2017	European Egyptian Pharmaceuticals Ind	4.. 424. 00	J05AX15
14	RK-LS 5№023276	Daclatasvir	VIRDAK	Registration	03.10.2017	Hetero Labs Limited		J05AX14
15	RK-LS 5№024005	Sofosbuvir	VALDIS	Registration	24.01.2019	SHROOQ PHARMACEUTICAL (Pvt.) Ltd.		J05AP

[103] Cost per a set of tablets.