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ANTIRETROVIRAL DRUGS PROCUREMENTS TO ADDRESS HIV TREATMENT AND DRUGS PROCUREMENTS TO ADDRESS VIRAL HEPATITIS C TREATMENT IN THE REPUBLIC OF KAZAKHSTAN FULL STUDY REPORT FOR THE YEAR 2019

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АНТИГЕПАТИТ'С
AGEP'C

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AUTHORS AND ACKNOWLEDGEMENTS

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DISCLAIMER

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Under no circumstances, the references made to any treatment regimen in this report should 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

ANTIRETROVIRAL DRUGS PROCUREMENTS TO ADDRESS HIV TREATMENT

INTRODUCTION

The HIV epidemic is maintained at the concentrated stage in Kazakhstan. As of December 31, 2019, the estimated number of people living with HIV has reached 31,378. A total of 36,584 cases of HIV infection were registered as of December 31, 2019. 25,753 PLHIV are aware of their HIV status, of which 21,951 (69.95%) are registered with dispensaries. 17,535 people (55.88% of the estimated number and 79.88% of those registered) receive ARVs. 13,605 patients (43.35% of the estimated number and 77.58% of those taking ART) have an undetectable viral load.

The prevalence rate of PLHIV per 100,000 populations is 138.2 (minus those who died of HIV/AIDS, anonymously identified individuals and foreign nationals as of December 31, 2019). The highest prevalence of PLHIV was registered in the Pavlodar region (279), Karaganda region (258), Almaty (228), East Kazakhstan region (221), North Kazakhstan region (218), Kostanay region (215), and Shymkent (170). The incidence rate per 100,000 population is 18.9.

Mortality Rate

In 2019, AIDS-related mortality reached a rate of 10.6 per 1000 PLHIV (11.1 per 1000 PLHIV in 2018). Thus, the death rate from AIDS in Kazakhstan decreased in 2019.

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 2020, a new clinical protocol was launched, based on the WHO guidelines (2019) and the European treatment guidelines (2019).

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

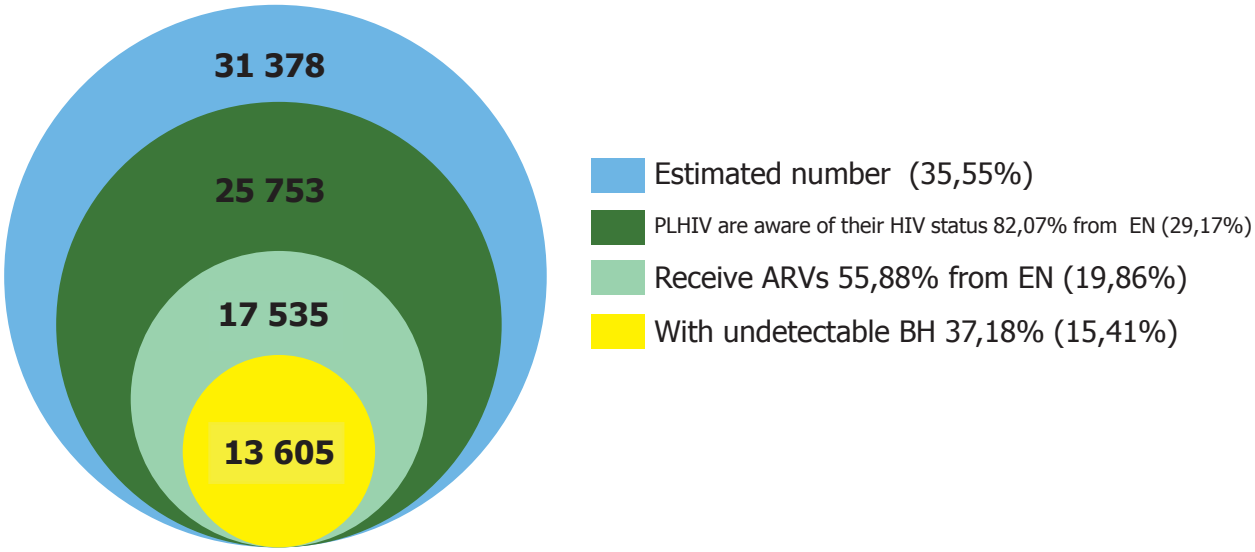
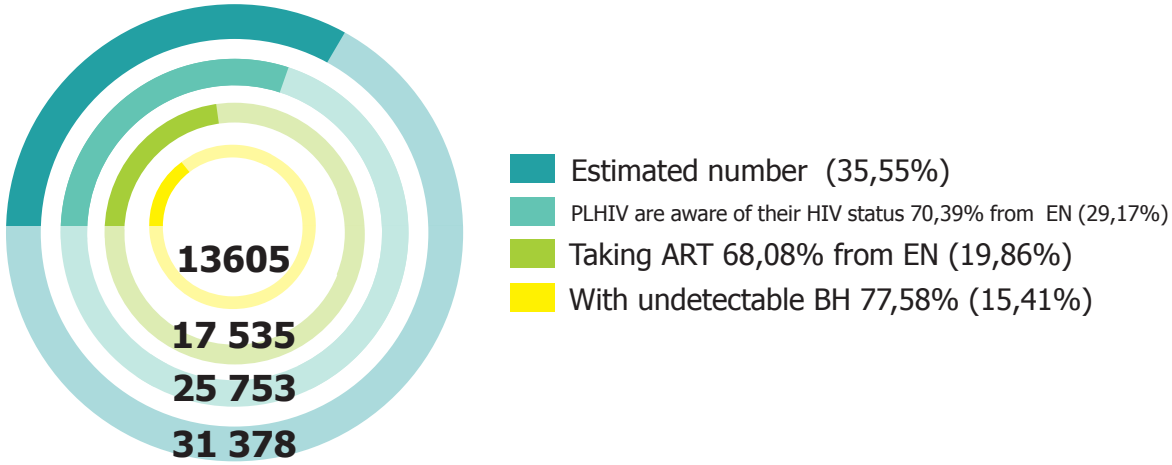


Figure 2. The HIV Treatment Cascade



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 2019 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 2019 and provided by the Single Distributor and the Kazakhstan Scientific Center for Dermatology and Infectious Diseases..

The authors of the report studied the legislation governing examination, registration of medicines, the process of drawing up a budget proposal and the procurement process for ARV drugs.

The report is based on information obtained from open sources such as https://medelement.com/, https://www.ndda.kz/.

OVERVIEW OF THE REGULATORY FRAMEWORK

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

- 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 July 7th, 2020, No. 360-VI.

ARV therapy is prescribed in accordance with the Clinical protocol for the diagnosis and treatment of HIV infection in adults No 97 of June 11, 2020.

BUDGET LEGISLATION

In Kazakhstan, medicines for treating HIV are purchased by budgetary funds. The budget funds come from the national budget to the Social Health Insurance Fund (SHIF) in the form of budget transfers[1].

The Ministry of Health in coordination with the Social Health Insurance Fund develops a budget request[2] that includes all necessary calculations such as number of patients, required amount of medicines, etc. Subsequently, the budget request should be addressed to the Ministry of Finance by May 15 of the present year, which draws up and submits the national budget for approval by the National Budget Commission.

Review of the proposed budget should be completed by August 1 of the current financial year, after which and no later than August 15 it should be submitted 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 should be issued within 7 calendar days since the law being signed by the President of the Republic of Kazakhstan. A 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 should be calculated at the budget proposal stage based on data from previous periods. This calculation provides SHIF and its results are not published. In addition, amendments may be made to the budget during the year due to savings and additional requirements.. In this regard, it is not possible to provide reliable data data on the budget allocated for HIV drug provision by years.

[1] The Budget Code of the Republic of Kazakhstan №95-IV of December 4, 2008, Art. 35, P.2-2.
[2] 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 AUTHORIZATION PROCEDURES

According to the Republic of Kazakhstan's current legislation, 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 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 form, dosage, and type of packing;
5) medicines registered earlier in the Republic of Kazakhstan and produced by other manufacturing organizations, in other 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; and
7) medicines of single marketing authorization holders produced in different countries at different production sites.

It is allowed to import into the Republic of Kazakhstan unregistered drugs based on a conclusion (an 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.

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

A required condition for the state registration, re-registration, or modification of the drug registration profile is examining the medicinal product[3], carried out by the National Centre for Expertise of Medicines, Medical Devices, and Medical Equipment.

A required condition for the state registration, re-registration, and modification of the drug registration profile is a **Good Manufacturing Practice (GMP)**[4] of manufacturing organizations.

The expert examination of drugs, with the exception of drugs manufactured in the Republic of Kazakhstan or ICH countries[5], shall be carried out within a period not exceeding 210 calendar days[6].

The expert examination of drugs for state registration depends on the types of proposed changes and shall be carried out within a period from 30 to 120 calendar days.

[3] Order of the Ministry of Health of the Republic of Kazakhstan dated November 18, 2009 No. 736 «On Approval of the Rules for Expertise of Medicines, Medical Devices and Medical Equipment».
[4] 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 the obtaining marketing authorization, re-registration and modification of the registration profile of medicinal products, medical devices and medical equipment».
[5] The countries of the International Conference on Harmonization of Technical Requirements for Registration of drugs for medical use
[6] 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»

The examination of drugs produced in the Republic of Kazakhstan shall be carried out for 180 calendar days.

The examination of drugs produced in the ICH countries shall be carried out for 180 calendar days.

After the 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, the registration, re-registration or modification of the registration profile shall be performed by the Committee of Pharmacy of the Ministry of Healthcare of the Republic of Kazakhstan[7].

NATIONAL BUDGET PROCUREMENT PROCEDURES FOR THE MEDICINAL PRODUCTS, INCLUDING ANTIRETROVIRAL AGENTS AND HCV DRUGS

The procurements of MPs (Medicinal Products), including antiretroviral agents, under the framework of the SFMA (Statutory Free Medical Assistance) and in the CSHI (Compulsory Social Health Insurance) system are excluded from the public procurement legislation of the Republic of Kazakhstan[8]. The MP procurement procedures are set out in the Governmental Decree of RoK 719[9].

The SFMA MP and additional medical care are purchased under the INN (the international non-proprietary names) and the TN (trade names) if any individual patient intolerances. In the case of the procurement of a poly-component medicinal drug, its composition must be indicated[10].

Medicines are purchased at maximum prices, not exceeding the limits established by an authority for the rational use of funds allocated for SFMA medicines' procurement. In 2019, the Sole Distributor List's price limits had been approved by the order of the Ministry of Health of the Republic of Kazakhstan No. 434.

In the absence of quoted prices for the SFMA medicines, the price ceiling is not determined, and no procurement is carried out under the SFMA[11].

Limit prices for TN are regulated by order of the Ministry of Health of the Republic of Kazakhstan No. 931[12].

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

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

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[7] 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». Order of the Ministry of Health and Social Development of RK dated November 18, 2009 No. 735 «On approval of Rules for obtaining the marketing authorization, re-registration and modification of the registration profile of medicinal products, medical devices and medical equipment».
[8] Code of the Republic of Kazakhstan «On the Health of the People and the Health System», Art. 2,p.2, September 18th, 2009.
[9] 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 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», dated by July 8, 2015.
[10] Code of the Republic of Kazakhstan «On the Health of the People and the Health System», Art. 76
[11] Order of the Ministry of Health of the Republic of Kazakhstan No. 53 of February 8, 2018 "On Amending Order of the Acting Minister of Health and Social Development of RK dated July 30, 2015 No. 639 «On the Pricing Policy for Medicines and Medical Products within the Statutory Free Medical Care»
[12] 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"

In Kazakhstan, the Single Distributor is SK-Pharmacia LLP, 100% of which belongs to the state.

The SD and Compulsory Medical Insurance Fund (CMIF) agree to provide the SD services within the SFMA and CSHI systems in the regions, cities of republican significance, capital, and healthcare entities.

The SD purchases ARV drugs as follows: through a two-stage tender; from a 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 emergencies; through a special procedure under long-term supply contracts from suppliers who intend to establish the manufacture of medicinal drugs or having a production of medicinal products; through a special procedure under long-term supply of original patented medicines from contract manufacturing customers.

For procurement under the SD list, customers (government agencies, Compulsory Medical Insurance Funds, and medical organizations executing government order) submit applications to the SD, which are the basis for the SD procurements.

Two-Stage Tender:

An announcement of a two-stage tender is published on the SD website.

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

If a tender purchase using a two-stage tender method or any of its lots is declared invalid, the SD 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 supply contract price. The SD forms a protocol on the procurements' results on its website and concludes a supply contract.

One of the procurement principles in purchasing medicines is domestic producers and/or manufacturers of the Eurasian Economic Union member states.

The following are the measures that are used to support DPs (domestic producers) and/or manufacturer of the Eurasian Economic Union member states:

In case of participation in the DP tender, the tender application of which meets the procurement rules' requirements, 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 the case 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. Since February 2018, this company is legally entitled to exceptional opportunities not to comply with other generics' pricing rules. The only obligation of DP is to reduce the price by 5% annually for 5 years.[13]

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

Single Source Procurements:

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 a potential supplier that is a foreign manufacturer, or a domestic manufacturer of drugs that do not have analogues registered in the Republic of Kazakhstan in terms of INN and (or) characteristics.

6) when purchasing through international organizations established by the General Assembly of the United Nations, in agreement with the authorized body of the health care system, on the basis of international treaties (agreements) ratified by the Republic of Kazakhstan, as well as international treaties signed for their implementation.

7) when purchasing medicines and medical devices and (or) pharmaceutical services up to ninety-day needs of their total annual volume, in the case when the submission of TOTAL to a two-stage tender passes to 2019.

[13] 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».

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: the existence of registration, conformity of labeling, consumer packaging and instructions, the existence of a registered price for a trading name;
- Shelf life and transportation conditions following 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.
- on behalf of the authorized body of the health care system, it is allowed to purchase medicines that are not included in the list of a single distributor in cases of a threat to the sanitary and epidemiological well-being of the population.
- **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; and

2) prevention and elimination of emergency consequences.

A special procedure for long-term supply contracts with suppliers who intend to set up production of drugs or have production of drugs.

The conclusion of a long-term contract for the supply of drugs is impossible if the drugs are registered by two or more DPs at the time of placing the advertisement.

In addition to purchasing through a SD at the expense of targeted current transfers from the national budget, ARV drugs can also be purchased at the expense of the local budget, in cases where the drug is included in the SFMA list but not included in the list of a Single Distributor[14].

RESTRICTIVE LISTS OF MEDICINES IN THE REPUBLIC OF KAZAKHSTAN

In the Republic of Kazakhstan, medical care is provided in the following amounts[15]:

1) basic – the statutory free medical assistance (SFMA),

2) additional medical care, including:
   - medical assistance in the system of compulsory social health insurance (CSHI)[16]
   - medical assistance as part of voluntary medical insurance[17].

[14] 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.

[15] 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

[16] The Law of the Republic of Kazakhstan «On Compulsory Social Health Insurance»;

[17] The Law of the Republic of Kazakhstan «On Insurance Activities»

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

1. Kazakhstan's National Medicinal Formulary, Order of the Minister of Health Social Development of the Republic of Kazakhstan No 931[18]
2. 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[19]
3. List of medicinal products to be purchased by the SD for 2019 with the indication of price ceilings, the Order of the Minister of Health of the Republic of Kazakhstan No434[20]

Treatment of drugs not included in these lists is carried out on a paid basis at the expense of patients.

Kazakhstan's National Drug Formulary[21] is a list of medicines with proven clinical efficacy and safety, containing information on medicines and prices, which is an obligatory basis for developing medicinal formularies of healthcare organizations drug procurement lists within the framework of SFMA and CSHI[22]. The Kazakhstan National Pharmaceutical Formulary includes all registered drugs, except for the following combinations: Atazanavir/Ritonavir, Lamivudine/Tenofovir/Efavirenz, Lamivudine/Tenofovir disoproxil.

However, not all formulary drugs (order No. 931) were included in the list of the SFMA and CSHI for 2019 (the Order No666) and ED list (the Order 434) which does not allow the purchase of all registered drugs.

For the first time, these lists included: **Lamivudine, Abacavir, Dolutegravir; Darunavir, Cobicistat; Tenofovir, Emtricitabine, and Rilpivirine.**

The following drugs are absent in all or several lists:

- Atazanavir / Ritonavir (not included in any list)
- Lamivudine / Tenofovir / Efavirenz (not included in any list)
- Lamivudine / Tenofovir disoproxil (not included in any list)
- Raltegravir (not included in the Order No. 666)
- Fosamprenavir (not included in the Orders No 666 and No 434)
- Rilpivirine (as a mono-drug is not included in the Orders No 666 and No 434)
- Ritonavir (as a mono-drug one is included in the Orders No. 666 and No. 434)

[18] 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"
[19] 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»
[20] Order of the Ministry of Health of the Republic of Kazakhstan No. 434 dated July 18, 2018, «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 2019»
[21] 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
[22] The Code on People's Health and Health Care System», Article.1, p.1, 61-1

ARV-MEDICINES IN KAZAKHSTAN

As of November 10, 2018, 27 INN (80 TN) were registered in the Republic of Kazakhstan, excluding various dosages and dosage forms[23].

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. Atazanavir / Ritonavir and Fosamprenavir are not used to treat patients.

Of the second generation NNRTIs, Rilpivirine and Etravirine are registered in Kazakhstan. Both drugs are used in small volumes due to the high cost and characteristics of the drug (Etravirine). Doravirin is not registered in Kazakhstan.

In 2019, Odefsey (Emtricitabine, Tenofovira alafenamide and Rilpivirine) and Simtuza (Emtricitabine, Tenofovira Alafenamide, Darunavir and Cobicistat) were registered, representing the first fixed combinations with TAF in Kazakhstan.

Annex No1 - Table 1. List of registered ARV medicines in Kazakhstan[24].

Annex No6 - Table 6. List of registered medicines to treat HCV in Kazakhstan[25].

[23] http://www.dari.kz/category/search_prep
[24] The list of registered drugs on 10.11.2019, available at: http://www.dari.kz/category/search_prep, https://drugs.medelement.com
[25] 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/

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

2019 was a transitional period for the Republic of Kazakhstan in terms of prescribing treatment regimens. The reason for this was that clinical protocols from 2017 were officially in force in 2019. At the end of 2019, new protocols were drawn up and passed the approval stage, developed based on the latest WHO recommendations (July 2019)[26] and the European AIDS Clinical Society (EACS)[27]. As a result, the document came into force only on June 11, 2020[28]. Simultaneously, an increase in the number of patients taking drugs recommended by the new protocols has already occurred in 2019.

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

	Combination of NRTIs		Third drug
	First drug	Second drug	
Preferred regimens	3TC (or FTC)	TDF (or TAF)	DTG
	3TC (or FTC)	TDF (or TAF)	BIC
	3TC	DTG	
Alternative regimens	3TC (or FTC)	TDF	EFV (400,600) or RPV
	3TC	ABC	EFV (400,600) or RPV
	3TC	ABC	DTG
	3TC (or FTC)	ABC (or TDF)	RAL
	3TC (or FTC)	TDF (or TAF)	EVG/c
	3TC (or FTC)	TDF (or TAF or ABC)	DRV/c or DRV/r
Special conditions	RAL	DRV/r or DRV/c	

First-line regimens based in part on the latest WHO review and in part on the EACS recommendations:

- Recommended regimen with 2 NRTIs + DTG is in both of the above mentioned documents.
- Added regimens with 2 NRTIs + BIC, 2 NRTIs + RPV, as well as a two-drug regimen (3TC + DTG). These regimens are only mentioned in the guidelines of the European AIDS Clinical Society.
- Difficult to speculate about the differences between the first and second drugs compared with the European experience, as the EACS guidelines only include the concepts of recommended and alternative schemes.
- The difference from the European guidelines is the absence of the NNRTI Doravirin

[26] Update of recommendations on first- and second-line antiretroviral regimens, 17.07.2019. WHO https://www.who.int/publications/i/item/update-of-recommendations-on-first--and-second-line-antiretroviral-regimens
[27] European AIDS Clinical Society (EACS) Guidelines, November 2019, version 10.0. https://www.eacsociety.org/files/eacs_gudelines_2019_rus.pdf
[28] Clinical protocol for the diagnosis and treatment of HIV infection in adults No. 97 dated 06/11/2020

(DOR) in National Treatment Protocols.

- When comparing national protocols with the 2019 WHO review of recommendations, in the special circumstances of the first line of the National Protocols, AZT is absent, and DRV / c, DRV / r are included. Also, most of the National Protocol's alternatives are assigned to special circumstances in the WHO recommendations.

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

Preferred regimens	Alternative regimens
3TC + AZT+DRV/c	AZT + 3TC + ATV/r (or LPV/r)
3TC + AZT + DTG	AZT + 3TC + ATV/r (or LPV/r or DRV/c)
3TC (or FTC) + TDF + DTG	3TC (or FTC) + TDF+ ATV/r (or LPV/r or DRV/c)

Second-line regimens are nearly in line with the latest WHO recommendations (2019). The exception is Atazanavir (ATV), which has been moved from the preferred second-line regimens to alternative regimens in the National Protocol.

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

DRV/r or DRV/c + DTG (or RAL) ± 1-2 НИОТ

DRV/r or DRV/c + 2НИОТ ± ННИОТ

DTG+RPV

The third-line therapy in the National Protocol includes the regimens recommended by the EACS in terms of "gentle" strategies: DTG + RPV.

The key directions of changes in the National Protocol are in line with the latest WHO recommendations (July 2019), namely, an increase in the number of people consuming Dolutegravire and Efavrenze 400 mg, as well as a reduction in the number of patients on «old» drugs as the following:

- Dolutegravir (DTG) is present in the preferred first-line regimen of the 2020 National Protocols and the preferred second-line regimen if the first regimen does not include Dolutegravir. In 2019, DTG was purchased for 1905 estimated treatment courses, 37.28% higher than in 2018.
- Efavirenz 400 is not registered in Kazakhstan; Efavirenz 200 was purchased in 2019 for regimens with this dosage. 521 patients used Efavirenz 400 mg.
- The number of purchased courses has been decreased: Zidovudine/Lamivudine (by 39.11% compared to 2018), Nevirapine (by 85.53% compared to 2018), Lopinavir/Ritonavir (by 25.77% compared to 2018).

ANTIRETROVIRAL DRUGS PROCUREMENT IN 2019

According to the official response from SK-Pharmacia, the total amount of ARV drugs procurement for 2019 was 5,100,000,000 tenge or 13,324,624.42 USD[29].

MECHANISMS OF PROCUREMENT

In 2019 the antiretroviral drugs (hereinafter referred to as ARV drugs) were purchased through a Sole Distributor - SK-Pharmacy LLP.

In 2019, 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 analogs in Kazakhstan in terms of INN and (or) drug's characteristics); and
- free of charge (humanitarian supplies).

Not all of the existing procurement methods are publicly available. In 2019, information on only two procurement methods was published on the SK-Pharmacy website, namely:

1. National tender - 3-4 original drugs, most of which are intended for children with HIV. The lack of competition distinguishes the method since only original drugs are involved;
2. Purchase within the framework of long-term supply agreements from domestic manufacturers (3-4 drugs produced by local suppliers).

686 300 608.33 KZT or 1 793 078.01 USD was spent on these two methods. This means that only 13.45% of all purchases ARV drugs are available for public monitoring.

Inquiries to SK-Pharmacy made it possible to obtain information on the total amount of purchases of ARV drugs and the number of purchased drugs within the other procurement methods (UNICEF, non-analog drugs, and humanitarian supplies). Information on prices of purchased ARVs was not provided due to a new clause on the confidentiality of information on procurement prices. Now, this information is confidential for 3 years. It is important to note that this rule was introduced at the level of contracts with suppliers, but is not included in the national legislation, which contradicts the regulations on openness and accountability of procurement within the guaranteed volume of free medical care.

Annex 3 below indicates all types of medications purchased by the SD for 2019 as of December 2019.

It should be noted that the Ministry of Health of the Republic of Kazakhstan purchases only original drugs to treat children. In this regard, the Single Distributor conducts tender procedures to provide children separately. For the rest of the patients, both originals and generics are purchased. As a result, both originals and generics with different trade names can be supplied under the same drug names. Accordingly, they can be procured using various procurement mechanisms.

The following drugs in the amount of 385,201,274.13 tenge or 1,006,404.37 US dollars were purchased through a two-stage tender:

[29] Average annual dollar exchange rate for 2019 = 382.75 tenge, https://online.zakon.kz/m/document/?doc_id=30157076#sub_id=2019

Table 3. ARVs procured for 2019 through a two-stage tender

INN	TN	Packa-ging	Manu-facturer	Purchase volume	Supplier price, tenge per unit	Supplier price, tenge per package	amount at supplier price (KZT)	amount at supplier price (USD)	Price comparisons 2019 to 2018	Original / generic
Lopinavir + Ritonavir	Aluvia	60	AbbVie Deutschland GmbH & Co.	141 360	59,78	586,80	8 450 500,80	22 078,38	0%	original
Lopinavir + Ritonavir	Aluvia	120	AbbVie Deutschland GmbH & Co.	1 672 800	173,77	20 852,40	290 682 456,00	759 457,76	0%	original
Lopinavir + Ritonavir	Aluvia	120	AbbVie Deutschland GmbH & Co.	393 120	173,77	20 852,40	68 312 462,40	178 478,02	0%	original
Lopinavir + Ritonavir	Kaletra	1	AbbVie Biopharma-ceuticals GmbH.	1 110	3 195,11	3 195,11	3 546 572,10	9 266,03	0%	original
Nevirapine	Vira-mune	60	Boehringer Ingelheim Ellas A.E.	46 800	144,42	8 665,20	6 758 856,00	17 658,67	▲ 0,30%	original
Nevirapine	Vira-mune	1	Boehringer Ingelheim GmbH	2 233	3 336,51	3 336,51	7 450 426,83	19 465,52	Not purchased in 2018	original
TOTAL:							385 201 274,13	1 006 404,37		

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.

There was no price drop in comparison with 2018.

4 drugs for ARV therapy were purchased under long-term supply contracts from Abdi Ibrahim Global Pharm LLP (AIGF): Abacavir, Zidovudine, Zidovudine + Lamivudine, Lamivudine. The total amount was 301,099,334.20 tenge or 786,673.63 US dollars. For this type of ARV drugs purchase, 1 billion less was allocated than in 2018, which indicates savings in the state budget.

Table 4. List of ARVs purchased under long-term supply agreements with Abdi Ibrahim Global Pharm

INN	TN	Packa-ging	Purchase volume	Supplier price, tenge per unit	Supplier price, tenge per package	amount at supplier price (KZT)	amount at supplier price (USD)	Price comparisons 2019 to 2018
Abacavir, tablet 300 mg	Virakar	60	6420	554,21	33 252,60	3 558 028,20	9 295,96	▼5,32%
Zidovudine, capsule 100mg	Zidoas	100	17800	106,15	10 615,00	1 889 470,00	4 936,56	0%
Zidovudine+ Lamivudine, tablets 300 mg/150 mg	Duolazide	60	1003200	279,89	16 793,40	280 785 648,00	733 600,65	▼ 62,96%
Lamivudine, tablet, 150 mg	Lamias 150	60	36600	406,18	24 370,80	14 866 188,00	38 840,47	Not purchased in 2018
					TOTAL	301 099 334,20		

The table shows that the price of Duolazide has dropped significantly (by 62.96% compared to 2018), but it is still higher than the price of the original Combivir (by 31.54%). One of the reasons for the significant price reduction is the active advocacy work of non-profit organizations in the Republic of Kazakhstan. The price has decreased, and the purchased drug (by 41% compared to 2018). Monitoring data indicate that instead of the Lamivudine / Zidovudine combination, international organizations' recommended more modern drugs were used.

In 2019, some ARV drugs were purchased through UNICEF:

Table 5. ARV drugs purchased through UNICEF

INN	Trade name	Packaging ga	Manufacturer	Number of units	Original / generic
Abacavir, 300 mg	Ziagen	60	GlaxoSmithKline Pharmaceuticals S.A.	58860	original
Abacavir+ Lamivudine	Kivexa	30	GlaxoSmithKline Pharmaceuticals S.A.	53160	original
Abacavir+ Lamivudine	Kivexa	30	GlaxoSmithKline Pharmaceuticals S.A.	921210	original
Zidovudine, capsule, 100 mg	Retrovir	100	GlaxoSmithKline Pharmaceuticals S.A.	44700	original
Zidovudine+ Lamivudine	Combivir	60	GlaxoSmithKline Pharmaceuticals S.A.	134100	original
Lamivudine, 150 mg	Epivir	60	GlaxoSmithKline Pharmaceuticals S.A.	56580	original
Nevirapine, 200 mg	Nevivir	60	Hetero Labs Limited	88200	generic
Tenofovir+ Emtricitabine +Efavirenz	Efavirenz, Emtricitabine , Tenofovir Disoproxil Fumarate	30	Hetero Labs Limited	2468970	generic
Tenofovir, 300mg	Tenofovir Disoproxil Fumarate	30	Mylan Laboratories Limited	922140	generic
Emtricitabine + Tenofovir	Tenochop-e	30	Macleods Pharmaceuticals Lmt.	1321710	generic
Efavirenz, 600 mg	Efavirenz	30	Hetero Labs Limited	466020	generic
Efavirenz, 200 mg	Efavirenz (Efavirenz)	90	Strides Shasun Limited	154800	generic

11 types of drugs were procured through UNICEF. It is not possible to track trends in price changes due to the lack of information.

10 types of drugs were purchased under contracts for the supply of non-analog drugs.

[31] https://www.total.kz/ru/news/proisshestviya/zdravoohranenie_birtanova_27_ugolovnih_del_rassleduet_genprokuratura_date_2019_08_02_14_44_45?fbclid=IwAR0hHtJ_1-K_IkSbgoMH70GoQcWJNWmci5b79kX__D3IpSmJ9qkodskZ-fg

Table 6. ARV drugs purchased under agreements for the supply of non-analogue drugs

INN	Trade name	Packaging a	Manufacturer	Number of units
Abacavir, solution 20 mg/ml 240 ml	Ziagen	1	GlaxoSmithKline Inc..	1065
Abacavir+ Lamivudine+ Zidovudine, 300mg/150mg/300mg	Trizivir	60	GlaxoSmithKline Pharmaceuticals S.A.,	56280
Darunavir + Cobicistat, 800 mg/150 mg	Rezolsta	30	Janssen – Orto LLC,	250830
Dolutegravir, 50 mg	Tivicay	30	Glaxo Operations UK ltd.	37260
Dolutegravir, 50 mg	Tivicay	30	Glaxo Operations UK ltd..	658290
Zidovudine, solution 10 mg/ml 200 ml	Retrovir	1	GlaxoSmithKline Inc.., Canada	2727
Lamivudine, solution 5 mg/ml 240 ml	Zeffix	1	GlaxoSmithKline Inc..	3875
Lamivudine + Abacavir + Dolutegravir, 300 mg/600 mg/50 mg	Triumeq	30	Glaxo Operations UK ltd..	174720
Emtricitabine +Tenofovir+ Rilpivirine	Complera	30	Janssen-Cilag S A,	96240
Etravirine, 100 mg	Intelens	120	Janssen-Cilag S A,	8280
Etravirine, 200 mg	Intelens	60	Janssen-Cilag S A,	65520
Etravirine, 200 mg	Intelens	60	Janssen-Cilag S A,	94020

The most common schemes in the Republic of Kazakhstan, according to the Kazakhstan Scientific Center of Dermology and Infectious Diseases, were[30]: TDF / FTC / EFV, TDF / FTC + DTG ABC/3TC + DTG, TDF/FTC + LPV/r, AZT/3TC + LPV/r. DRV / c regimens have replaced DRV / r, as well as EFV 400 regimens. There were cases of non-compliance with National Protocols, but could be due to individual intolerance and resistance to some drugs.

Procurement monitoring data showed that according to the estimated number of annual courses (Appendix 5), the main drugs used in treatment regimens were: TDF + FTC + EFV, TDF + FTC, AZT + 3TC, TDF, LPV / r, EFV, ABC + 3TC, DTG, DRV / c, ABC + 3TC + DTG. This is generally consistent with the data presented in the table.

Table 7. Treatment regimens in Kazakhstan

№	Treatment Regimens	Number of Patients	Number of Patients 2019	Comparison 2019 vs 2018 (%)
1	2018	Number of Patients	524	+19,4%
2	2019	Comparison 2019 vs 2018 (%)	418	+18,75%
3	ABC/3TC+NVP (ABC+3TC+NVP)	139	133	-4,31%
4	ABC/3TC+TDF	26	3	-88,46%
5	AZT/3TC/ABC, (AZT/3TC+ABC), (AZT+3TC+ABC)	269	99	-63,19%
6	AZT/3TC+EFV (AZT+3TC+EFV)	827	418	-49,45%
7	AZT/3TC+LPV/r (AZT+3TC+LPV/r)	893	545	-38,96%
8	AZT/3TC+NVP (AZT+3TC+NVP)	717	225	-68, 61%
9	AZT/3TC+ETR		30	
10	TDF/FTC+EFV (TDF+FTC+EFV)	7233	**9343**	**+29,17%**
11	TDF/FTC+LPV/r	787	797	+1,27%
12	TDF/FTC+NVP	362	289	-20,16%
13	TDF/FTC/RPV		259	
14	ABC/3TC+DTG	428	783	+82, 94%

[30] The antiretroviral therapy regimens used in the period from 01.01.2019 to 31.12.2019 in Kazakhstan. Data for all categories of patients, including children. Kazakhstan Scientific Center of Dermatology and Infectious Diseases.

15	ABC+TDF+LPV/r	5		
16	TDF/FTC+ABC	17	7	-58, 82%
17	ABC/3TC+DRV/r	222		
18	ABC/3TC+DRV/c		207	
19	ABC/3TC+ETR		59	
20	TDF/FTC+DTG	880	**1361**	+54,65%
21	TDF+AZT+LPV/r	2		
22	TDF/FTC+DRV/r	559		
23	TDF/FTC+DRV/c		379	
24	TDF/FTC+ETR		76	
25	Other schemes	785	1580	+101,27%
	TOTAL:	14951	17535	+20,17%

COMPETITION IN THE COURSE OF BIDDING

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

This is, first of all, due to the following factors:

1) Support of domestic manufacturers within the framework of long-term supply contracts. There is no competition when purchasing drugs from domestic manufacturers (4 drugs) under long-term supply contracts. Delivery is carried out directly without tender procedures;
2) The need to purchase original drugs for children with HIV. During the tender procedures for 3 drugs for children, there was also no competition. As a result, prices for these drugs remained at the level of 2018.

Table 4 "Actual prices and contract amounts for ARV drugs purchased in 2019" in Annex 4 below provides detailed breakdowns for prices for each drug per year.

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 to treat 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 were provided 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; and
- tests for CD4 and viral load was not provided; laboratory and instrumental diagnostics as part of the guaranteed volume of medical care / compulsory health insurance were 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 healthcare institution worker. The consultant provides information on interruptions to the authorized representative of the Ministry of Health.

In 2019, the site pereboi.kz received 113 requests on the following issues:

- replacement of the scheme without medical indications - 34 complaints (Temirtau, Almaty, Pavlodar, Nur-Sultan, Ust-Kamenogorsk, Ekibastuz, Almaty region, and Aktau)
- lack of drugs due to late deliveries - 74 complaints (Temirtau, Almaty, East Kazakhstan region, Taraz, and Pavlodar)
- side effects - 2 complaints (Temirtau, Astana)
- inconvenient schedule of doctors' appointments at the center - 3 complaints (Almaty)

The main drugs for which interruptions were recorded in 2019: Dolutegravir, Tenofovir / Emtricitabine, Abacavir / Lamivudine, Tenofovir / Emtricitabine / Efavirenz. In most cases, interruptions occurred due to the late conclusion of contracts with suppliers.

Also, for patients with hepatitis C, there is a feedback system on the Гепатитinfo[31] website, and a page in the FB[32]. The consultant reports information about the incident to a representative of the authorized body of the Ministry of Health of the Republic of Kazakhstan.

In 2019, there were appeals regarding the refusal to provide free diagnostics during the next examination and prescribing antiviral therapy. In such cases, the applicants were provided with information about their right to free diagnostics, including its expensive types. To address these issues, information was also passed on to heads of medical organizations and heads of health departments of cities and regions.

In 2019, a call center was launched under ED with a short number 14-39 to cover drug provision issues under the guaranteed medical insurance/compulsory medical insurance systems. For the period 01.01.2019 to 31.12.2019, 87 calls were received regarding the Sofosbuvir and Daclatasvir provisions. Not all inquiries were complaints. Karaganda region was the leader in terms of the number of general requests - 22 calls. Due to the refusal to issue Sofosbuvir and Daclatasvir, the Almaty region was in the lead - 2 appeals out of 17 regions and cities.

Call center operators registered all calling patients. A "Client Card" was created for each patient, which indicated the patient's personal data and other information. In case of any problems with drug supply, the card was sent to the Department of Drug Supply, the ED Department of Logistics, and the designated medical facility to resolve the issue further.

[31] www.hepatit.kz
[32] https://www.facebook.com/agepckz/

KEY FINDINGS:

- In 2019, the number of registered PLHIV in Kazakhstan was 21,951 (69.95% of the estimated number); 17,535 people have received therapy at the end of 2019 (55.88% of the estimated number, 79.88% of those registered). The number of patients with undetectable viral load due to ART was 13,605 (43.35% of the estimated number, 77.58% of the number of PLHIV taking ART).

- In 2020, new Clinical Protocols were approved, including recommendations of the WHO (2019) and EACS (2019). The updated protocols expanded the list of ARV drugs and added modern drugs, including those combined with a regimen of 1 tablet once a day. The preferred ART regimen for adults was changed (the TDF/FTC/EFV regimen was changed to TDF/FTC + DTG and TDF/FTC/BIC); the preferred regimen for pregnant women was changed (the TDF + 3TC (or FTC) + EFV regimen was changed to TDF/FTC + DTG); the "gentle' therapy regimens (DTG + 3TC, DTG + RPV) were included.

- According to the latest review of WHO recommendations in July 2019, there was an increase in the number of people on Dolutegravir and Efavrenz 400 mg, as well as a decrease in the number of patients using "old drugs":

  1) In 2019, DTG was purchased for 1905 estimated treatment courses, 37.28% higher than in 2018.
  2) Efavirenz 400 was not registered in Kazakhstan; in 2019, Efavirenz 200 was purchased to form regimens with this dosage. The number of patients on the schemes with Efavirenz 400 mg was 521 people.
  3) The number of purchased courses decreased: Zidovudine/Lamivudine (by 39.11% compared to 2018), Nevirapine (by 85.53% compared to 2018), Lopinavir/Ritonavir (by 25.77% compared to the 2018 year).

- Purchased for the first time such new drugs as Tenofovir/Emtricitabine/Rilpivirine; Lamivudine/Abacavir/Dolutegravir; Darunavir/Cobicistat, which were included in the clinical treatment protocol.

- Due to the late compilation of restrictive lists and delays in contracting with suppliers, there were 113 reports of regimen change/refusal to dispense ARV drugs in 2019.

- A decrease in the price of Dualozide (Zidovudine / Lamivudine) of the domestic manufacturer Abdi Ibrahim Global Pharm was recorded. The price was reduced by 62.96% compared to 2018. Also, the number of purchased courses decreased by 39.11% compared to 2018.

- Due to restrictions on access to information on contracts between SK-Pharmacy and ARV drug suppliers, it is impossible to monitor 86.55% of the budget. This does not allow for a comprehensive assessment of the effectiveness of the funds spent and violates the Republic of Kazakhstan legislation[33].

[33] Law of the Republic of Kazakhstan «On Access to Information», Article 6.

FURTHER STEPS REQUIRED TO OPTIMIZE THE PROCESS OF ARV PROCUREMENTS

1) Bring the documents on the supply of ARV drugs in line with the Constitution of the Republic of Kazakhstan and the Law of the Republic of Kazakhstan "On Access to Information" to increase the transparency of spending the national budget.

2) Timely formation of restrictive lists, the timely conclusion of contracts to prevent arising interruptions with ARV drugs.

3) Revision of support measures for domestic manufacturers to optimize ARV therapy costs, reduce prices, and increase the number of patients on ART. The transition from long-term supply contracts (where it is impossible to influence price reduction) to support measures in the form of subsidizing factories with domestic producers' obligation to reduce prices.

4) Expansion of the range of international organizations providing services for the procurement of ARV drugs. At the moment, procurement is only possible through organizations established by the United Nations General Assembly.

5) Expansion of the range of prequalifications when purchasing through international purchasing agencies, since currently only WHO prequalification is accepted. Procurement of drugs with strict regulatory agency approvals (such as FDA and EMA) must be allowed. This measure will expand the range of suppliers of ARV drugs when purchasing through international procurement agencies.

DRUGS PROCUREMENTS TO ADDRESS VIRAL HEPATITIS C TREATMENT

INTRODUCTION

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

At the national level, monitoring and evaluating the preventive medical checkup coverage for viral hepatitis does not exist. By the time the text of this Report was being developed, and HCV Exchange Clinic Registry did not exist in Kazakhstan. This makes access to data difficult and does not allow for a comprehensive assessment of the prevalence proportion of viral hepatitis and the burden imposed on the country's public health system[34].

HCV Exchange Clinic Registry was not existed

According to an independent study[35], 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 in determining total antibodies to the hepatitis C virus (AntiHCV) in blood, which required further confirmation by the PCR method.

According to the Statistics Committee of the Ministry of National Economic of Kazakhstan[36], Kazakhstan's population was 18,653,500 as of February 1, 2020. Thus, the estimated number of people with antibodies to HCV can range from 858,000 to 1,120,000.

Below are the main statistical indicators for chronic viral hepatitis "C" (hereinafter referred to as CVHC) provided by the Ministry of Health of the Republic of Kazakhstan[37]:

1. According to the Republican Center for Electronic Health of the Ministry of Health of the Republic of Kazakhstan, the number of people with chronic viral hepatitis "C" as of December 31, 2019 is 27,369 people.
2. In 2019, 51 new cases of acute viral hepatitis "C" were registered (incidence per 100 thousand population 0.58) and 3 899 cases of CVHC (incidence per 100 thousand population 21.0).
3. The prevalence of CVHC is 21.0 per 100 thousand population (3 899 people).
4. The number of people with chronic hepatitis C who needed treatment in 2019 - 16,138; 15 389 patients were prescribed antiviral therapy.
5. In 2019, the treatment of 13,606 patients with CVHC was completed.
6. Of the 13 606 patients who completed treatment, a sustained virological response to antiviral therapy was observed in 13 206 (97%); no response was found in 70 patients (0.5%); studies did not fit in 330 (2.5%) patients.
7. No sustained virological response to antiviral therapy was recorded in 70 patients.

[34] Resolution of the chief medical officers, the Workshop on Gastroenterology and Hepatology Issues, March 15, 2019.
[35] Journal «Medicine», No 9 (171), 2016, page 30-33 and No 5 (179), 2017, page 17-22.
[36] http://stat.gov.kz/faces/homePage?_afrLoop=4160784958148023#%40%3F_afrLoop%3D4160784958148023%26_adf.ctrl-state%3D1dtqvbru4f_4
[37] Letter of the Ministry of Health dated 03.04.2020, Reference No 22-1-22/ZT-И-1113

HEPATITIS C ANTIVIRAL LONG-TERM TREATMENT

Since 2011, the procurement of antiviral drugs for adults and children has been provided entirely by public funds in Kazakhstan. Medical treatment of Kazakhstan citizens infected with HCV has been 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 of the Minister of Health and Social Development of the Republic of Kazakhstan dated May 21, 2015 No. 367 "On approval of the list of socially significant diseases and diseases that pose a danger to others", Order "On amendments to the order of the Minister of Health and Social Development of the Republic of Kazakhstan dated May 21, 2015 No. 367 "On approval of the list of socially significant diseases and diseases that pose a danger to others".
10) 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.

Table 6 in Annex 6 provides the list of registered medicines for the HCV treatment in Kazakhstan". Source: The web-site of the National center for registration of drugs and medical devices of the MH RoK[38]; Kazakhstan National Drug Formulary (KNDF) of the MH RoK[39]. The

[38] http://www.ndda.kz/
[39] http://www.knf.kz/index.php/kz/

Joint Commission approved the latest "Clinical Protocol for the Treatment of Viral Hepatitis "C" in the Adults"[40], (hereinafter – the Protocol) 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.

The Protocol is based on the recommendations of the WHO, EASL[41], AASLD[42] provided in 2016. 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 pangenetic (for all genotypes) regimen of HCV treatment such as the Sofosbuvir and the Daclatasvir.

According to the Ministry of Health Order[43], all Kazakhstan citizens 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.

INDICATIONS FOR THE HEPATITIS C ANTIVIRAL THERAPY

Order of priority	Group of patients	Strength of recommenda-tions
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

The Protocol consists of 16 regimens of the HCV antiviral therapies, including the pangeno-typical 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.

[40] 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

[41] The European Association for the Study of the Liver

[42] The American Association for the Study of Liver Diseases

[43] The Order No.666 of the MH of RoK dated by August 29, 2017.

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
		24-72 weeks 5	48-72 weeks 5	Not approved

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 weeks1	24 weeks or + RBV 12 weeks
	SOF/VEL*	12 weeks		24 weeks or + RBV 12 weeks
Alternative HCV regimens	SOF*+RBV	12 weeks2	24 weeks	24-48 weeks
	Peg-IFNα+RBV	24-48 weeks3	24-48 weeks3	Not approved

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 weeks1	12 weeks1	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 2019

According to applications received from medical organizations, 884, 7 mln. tenge was allocated from the republican budget for 2019 for outpatient drug provision within the guaranteed volume of medical care/compulsory medical insurance for patients with viral hepatitis.

In 2019, medical organizations sent an application to the Social Health Insurance Fund for **8 93 918 115.95** tenge to pay for viral hepatitis patients' medicines.

According to the information system "Pharmaceutical provision" (ISLO), for the period from January 1 to December 31, 2019, for the disease "Chronic viral hepatitis C, including the stage of liver cirrhosis," the amount of paid prescriptions was 535 176 653, 58 tenges; for the disease "Viral hepatitis B with and without delta agent" the number of prescriptions paid was **358,741,462, 37** tenge.

In 2019, the Single Distributor procured the HCV drugs using only one method - through UNDP[44].

Following 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 LS (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, based on the international treaties (agreements) ratified by the Republic of Kazakhstan, and the international treaties signed for the implementation thereof, through a 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[45].

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[46]:

1. Drugs and medical products are imported into the Republic of Kazakhstan in the manner determined by a competent authority, under the customs legislation of the Republic of Kazakhstan and (or) the Eurasian Economic Union;
2. Medical drugs and medical products that are not registered in the Republic of Kazakhstan may be imported to the Republic of Kazakhstan based on 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, except for medical drugs and medical devices under long-term medical drugs and medical products supply contracts.

According to the Order No. 451[47], 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 2019.

[44] United Nations Development Program
[45] http://procurement-notices.undp.org/view_notice.cfm?notice_id=44544
[46] 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
[47] Order of the Minister of Health and Social Development of the Republic of Kazakhstan dated May 21, 2015 No. 367 «On approval of the list of socially significant diseases and diseases that pose a danger to others.»

Antiviral drugs purchased by the SD through UNDP in 2019

INN	DOSAGE FORM	BRAND NAME	PACKING	NUMBER OF UNITS	NUMBER OF PACKAGES	SUPPLIER
SOFOSBUVIR 400 mg	film-coated tablet	MYHEP	28	929 180	33 185	UNDP
DACLATASVIR 60 mg	film-coated tablet	MyDekla	28	929 180	33 185	UNDP

The share of each drug in the total budget

INN	BRAND NAME	MANUFACTU-RER	NUMBER OF UNITS	AMOUNT AT SUPPLIER PRICE, KZT	AMOUNT AT SUPPLIER PRICE, USD	SHARE OF TOTAL PURCHASE (%)
SOFOSBUVIR	MYHEP	MYLAN	929 180	33 627.025	988 647.52	100%
DACLATASVIR 60 mg	MyDekla	MYLAN	929 180	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 2019", 1 tablet of Daclatasvir is additionally provided with each unit of Sofosbuvir[48].

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	PACKAGE,	28	346,19 / 1,064[49]	9 693,32/ 29,79	29 076.96/ 89,37
DACLATASVIR 60 mg	MyDekla	28	00	00	0

Antiviral drug purchased by SD from a domestic manufacturer for 2019

INN	DOSAGE FORM	BRAND NAME	PACKING	NUMBER OF UNITS	NUMBER OF PACKAGES	SUPPLIER
RIBAVIRIN 200 mg	Film coated tablet	RIVIRIN	30	264 994	8 833	Abdi İbrahim Global Pharm,LLP

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[50]	1023.00/2.76	2866.92/7,75

[48] Letter of the Pharmacy Committee of the Ministry of Health of the Republic of Kazakhstan dated June 26, 2018 No. 3Т-Б-143; dated 07.02.2019 No. 3Т-Б-347
[49] At the rate of the 100% prepayment date, April 4th,2018; 1 USD = 325.37 tenge.
[50] 1 USD = 370 tenge

COMPETITION IN THE COURSE OF BIDDING

Since 2018, drugs used in the treatment of CVHC, sofosbuvir and daclatasvir have been purchased through the international organization UNDP. The cost of a 12-week course of treatment is $87.

In May 2019, Gilead Science Ireland UC included the Republic of Kazakhstan in a voluntary license for drugs for the treatment of CVHC. The inclusion of the country in a voluntary license means that the patent holder permits the Ministry of Health of the Republic of Kazakhstan to purchase not only expensive original drugs containing sofosbuvir separately, but also in combination with ledipasvir and velpatasvir for the treatment of CVHC, but also their much more affordable generic forms.

On May 31, 2019, a Memorandum of Understanding was signed between the Ministry of Health of the Republic of Kazakhstan and Gilead Science Ireland UC[51].

KEY FINDINGS

1. Sofosbuvir was purchased 91% below the ceiling price of the Ministry of Health of the Republic of Kazakhstan;
2. The cost of treating one patient per year has dropped from $ 5,757 in 2017 to $ 89 in 2019;
3. Since 2018, the coverage of providing patients with antiviral drugs has been increased in the Republic of Kazakhstan. According to the Order of the Ministry of Health of the Republic of Kazakhstan, drugs sofosbuvir and daclatasvir are provided to all patients registered on the "D" account, regardless of the stage and severity of the disease and in the absence of contraindications.
4. Access to data on the prevalence of CVHC in the Republic of Kazakhstan is difficult due to the lack of an established monitoring system.
5. In the Republic of Kazakhstan, since 2011, the procurement of antiviral drugs for adults and children has been fully funded from public funds. Medical assistance to citizens of the Republic of Kazakhstan infected with CVHC is carried out within the guaranteed free medical care volume.
6. Based on procurement data, 13,606 patients with CVHC were provided with pangenetic treatment in 2019. The percentage of therapy coverage from the number of patients with a confirmed diagnosis of chronic hepatitis C on the "D" register is 100%.
7. The price for a course of treatment per patient with the standard treatment regimen of sofosbuvir and daclatasvir (12 weeks) is $ 89, which is the lowest in the region.
8. The latest clinical protocol for the treatment of viral hepatitis C in adults dates from May 2017, contains all antiviral drugs on the market, and complies with WHO recommendations. The Protocol is going to be revised.

[51] https://sk-pharmacy.kz/rus/sotrudnichestvo/memorandum/

RECOMMENDATIONS

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.

FOCUS AREAS IN THE FUTURE

1) Promotion of the WHO recommendations[52] 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) Expanded coverage of the newly identified patients with essential medical drugs, including other treatment regimens.
6) Address the issue of Glecaprevir/Pibrentasvir drug:
   - inclusion of the Republic of Kazakhstan in the existing License; and
   - consideration of issuing a compulsory license.

[52] 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. A formula determines the scope of legal protection provided by a patent for a drug. 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. In contrast, 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 patent application filing date for an invention, the expert panel examines as to form thereunder (verification of the presence and compliance of the documents).

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

Examination of the application includes determining the possibility to classify the application as already existing patents; a search is made to determine compliance with the patentability criterion. 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.

A competent authority determines the list of objects for which favorable patenting conditions are provided.

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; and
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.

Срок действия патента и возможности для его продления

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 patent application 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). According to the definition of the Patent Law of Kazakhstan,[53] an invention is new if it is unknown from the information about the prior art; the invention has an inventive step; if it does not clearly follow from the information about the prior art for a specialist (including any information that became publicly available in the world before the priority date of the invention).

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, and the use of the protected process.

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; and
8) proposals contrary to public order, principles of humanity and morality.

In general, the procedure for granting patents meets the provisions of the Trade-Related Aspects of Intellectual Property Rights (TRIPS)[54]. However, the duration of a patent and a list of patentability criteria are not in the interests of patients. In particular, TRIPS does not contain recommendations to extend a patent's duration 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.

[53] http://adilet.zan.kz/rus/docs/Z990000427_
[54] Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)

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 treatment methods. This contributes to the emergence of secondary patents that extend patent protection, which also contributes to the monopoly of original manufacturerscturers.

Disputing a patent

During its entire validity period, a patent may be challenged and invalidated in whole or in part under a claim against its issuance in cases of non-compliance with the conditions of patentability.

Obviously, the Republic of Kazakhstan's legislation provides for the possibility to raise objections "against" the grant of a patent during the entire period of its validity. Simultaneously, the procedure for challenging a patent "after" the grant of a patent provides for litigation that can last for years. A more expedient method to prevent patenting of new drugs, the patentability of which raises questions, would be the possibility of filing objections to the grant of a patent at the stage of applying for registration of a patent, that is, "before" its registration.

Invalidation of a document of title and early termination thereof

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

If the title's document is partially invalid, a new patent is issued for the remaining protectable subjects.

Licensing agreements signed based on 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.

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

1) based on the patent owner's application 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 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 expiration date of the established payment term, within the established time period.

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

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

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).

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 judicial review:

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 ownership;
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 the employer
- On payment of compensation fees provided for by this law.

Claims for refusal to grant a patent are filed with the court after considering the relevant objections in the Board of Appeals.

Based on a court decision, the expert organization publishes information about the changes related to protection titles.

Prior-use right and temporary legal protection

A person who, before the priority date 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 identical solution took place, or the necessary preparations were made for this.

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

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 patent holder's application on granting the right to an open license may not be revoked and remains valid for three years from the date of its registration.

A person who has expressed a desire to acquire an open license is obliged to conclude an appropriate agreement with the patent holder in writing.

The court considers disputes over the terms of the contract.

Infringement of the exclusive rights of the patent holder

Infringement of the patent holder's exclusive rights 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.

(Legal practices: http://almaty.sud.kz/rus/news/sud-vosstanovil-narushennye-isklyuchitelnye-prava-na-patent)

FORCED NON-EXCLUSIVE LICENSE

The Forced license - a permit issued by state bodies to an interested person to use a patented invention without the consent of the patent owner in cases specified by law

Forced non-exclusive license (FNEL) is granted in the following cases[56]*:*

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 the 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 number of payments must not be below the license's market price, determined following 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 to export 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, following 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.

56 Patent Law of the Republic of Kazakhstan dated July 16, 1999 No. 427, part 4 of article 11

A court may cancel FNEL 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.

If the patentee, who cannot use the industrial property object without violating the rights of the owner of another title of protection, proves that his industrial property object is an important technical achievement and is of great economic importance over the industrial property object of the owner of another title of protection, the court may be a decision was made to grant him a forced non-exclusive license.

The right to use an industrial property object obtained based on this clause may be transferred only together with the assignment of a title of protection to the industrial property object connected with which this right was granted.

In obtaining a forced license, the holder also has the right to obtain a license to use the dependent invention in connection with which the compulsory license was issued

The forced license is one of the TRIPS flexible provisions tools, increasing the number of patients' access to the newest drugs for treating HIV at a 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.

In Kazakhstan, the Ministry of Health was actively involved in issuing a forced license for Dolutegravir in 2019 https://informburo.kz/novosti/britanskiy-postavshchik-otkazal-kazahstanu-v-skidke-na-preparat-dlya-pacientov-s-vich.html. On the part of non-profit organizations, assistance was provided in the analysis of legislative acts and the development of recommendations for changing the regulatory framework and including options such as issuing a forced license by the patent office in agreement with the Ministry of Health, with the appropriate justification of the feasibility of such issuance. Technical assistance was also provided in drafting a claim for a forced license. (http://itpcru.org/2016/07/01/modelnyj-isk-o-vydache-prinuditelnoj-litsenzii-na-arv-v-kazahstane/)

PARALLEL IMPORTING OF MEDICINES

Medical drugs are imported into the Republic of Kazakhstan's territory in the manner determined by a competent authority following the customs legislation of the Republic of Kazakhstan and (or) the Eurasian Economic Union[57].

Importation into the Republic of Kazakhstan's territory of the medical drugs, which did not undergo state registration in the Republic of Kazakhstan, is not allowed, except for the following cases[58]:

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.

It is prohibited to import into the Republic of Kazakhstan's territory as humanitarian aid medicines and medical devices that have not passed state registration, except certain cases determined by the authorized body.

Medicines and medical devices imported into the Republic of Kazakhstan's territory that do not meet the requirements of the Republic of Kazakhstan's legislation in the field of healthcare 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 that are licensed to manufacture medicines;
2) entities in the field of circulation of medical drugs that are licensed to wholesale the sale of medicines;
3) research organizations, laboratories for the development and state registration of medicines following 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 in the Republic of Kazakhstan;
5) healthcare organizations for medical activities.

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

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[59].

A trademark can be registered in any color or color combination[60].

The trademark owner has the exclusive right to use and dispose of his trademark concerning the goods and services specified in the certificate[61]. No one can use[62] 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 with 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[63].

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 Kazakhstan legislation will significantly reduce budget expenditures on the purchase of original drugs.

[59] 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.
[60] Information Letter No. 95 of the National Patent Office under the Cabinet of Ministers of the Republic of Kazakhstan dated January 19, 1995.
[61] 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.
[62] 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;
[63] 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.

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

1) the individual or entity who has been issued a forced license to use a medicinal product following the Patent Law of the Republic of Kazakhstan
2) the use, production, import, export, or distribution of a medical drug for non-commercial purposes.

Based on 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) Identifying actions that violate the requirements of the Republic of Kazakhstan's legislation in the field of competition protection.

The new version of the code abolished the clause on the disclosure and use of registration dossier data in case of "the need to protect public health in emergencies, or to ensure national security." Still, to resolve issues of providing patients with drugs, you can also use the clause on obtaining registration data a dossier under the issued forced license, which, according to patent law, can be issued in the interests of protecting the health of citizens. But even with such a proviso, the exclusivity of the data, in which within 6 years after the registration of the patent, the data on the new drug is closed, deprives other manufacturers of the opportunity to start registering generic versions, since the closed data of the original drug is used when submitting the registration dossier. The later generic companies start this work, the longer Kazakhstani patients will not see available drugs on the market.

It is in the interests of patients in Kazakhstan to abolish the data exclusivity regime to stimulate the entry of generic versions of drugs on the market, stimulate competition in the drug market and expand patient coverage with treatment, not only in the case of a compulsory license.

Until recently, there were no restrictions in the Republic of Kazakhstan regarding registration of generics. However, on March 1, 2020, the Enhanced Partnership and Cooperation Agreement between the European Union and its member states, on the one hand, and the Republic of Kazakhstan, on the other hand, entered into force. It included a provision prohibiting the issuance of a marketing authorization for a generic drug. It is worth noting that this Agreement will apply only to those medicines that will be registered after March 01, 2020, and does not apply to earlier applications.

So far, the courts of Kazakhstan are in no hurry to interpret the law towards generics producers. So, in the only case about which there is information in the public domain, the Supreme Court of the Republic of Kazakhstan recognized that registration of a generic drug during the period of data exclusivity is illegal[64].

[64] https://kplaw.kz/ru/publications/yuristyi-kassilgov-and-partners-i-legalmax-law-firm-uspeshno-zashhitili-prava-proizvoditelya-originalnyix-lekarstvennyix-sredstv-posredstvom-primeneniya-instituta-eksklyuzivnosti-dannyix-data-exclusivity

PATENT LINKAGE

The Patent Linkage concept 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 expiring the document of title for the original medical drug.

The applicant informs in writing about the non-infringement of the third party rights protected by a patent in connection with the registration of a medical drug.[65]

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.

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.

BOLAR PROVISION

Actions that are not recognized as an infringement of the exclusive rights of the patent holder.[66]

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

1) 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.

Actions during a state of emergency:

It is not recognized as a violation of the exclusive right of the patentee: the use of patented means in emergency circumstances (natural disasters, catastrophes, major accidents) with immediate notification of the patent owner and subsequent payment of proportionate compensation to the patent owner;

On March 1, 2020, an agreement on expanded partnership and cooperation between the European Union and the Republic of Kazakhstan entered into force[67], which regulated a number of measures on intellectual property.

[65] Order of the Minister of Health of the Republic of Kazakhstan dated May 27, 2019 No. KR DSM-87. On amendments to the order of the Minister of Health of the Republic of Kazakhstan dated November 18, 2009 No. 735 «On approval of the Rules for state registration, re-registration and amendments to the registration dossier of a medicinal product, medical devices and medical equipment», Chapter 2. Clause 13

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

[67] https://online.zakon.kz/document/?doc_id=37496546

Recommendations:

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

2) Introduce the concept of challenging a patent application "before" the grant of a patent.

3) Refuse to apply measures related to the seizure of a batch of drugs in the event of a patent holder's complaint about infringement of IP rights in the supply of generic drugs to ensure the statutory free medical assistance and CSHI.

4) Introduce the concept of "state use of inventions," i.e., to amend the legislation to allow the issuance of a forced license for medicines based on the order of the National Patent Office and the Ministry of Health for the benefit of public health.

5) Limit the prohibition on the use of exclusive data to the information that is directly contained in the registration dossier. For registration purposes, authorize the use of information on clinical trials that is in the public domain.

6) Limit the abuse of patent holders' exclusive rights in the form of actions that restrict competition.

7) Specify and supplement the provisions on the conditions of patentability concerning inventions in the field of pharmaceutical compositions:

   - conditions under which the use of signs related to the method of treatment or prevention of a disease is not allowed (for example, indication of doses, conditions or modes of use of the composition or drugs obtained on its basis),
   - conditions under which it is not allowed to use information that is not directly related to the composition to characterize a composition (for example, conditions and modes of using this composition in any process, method); quantitative (measured or calculated) parameter characterizing one or more properties of the composition, in cases where this parameter is a distinguishing feature in the characteristic of the composition in an independent claim (for example, parameters of lamination strength, resistance to stress cracking, pharmacokinetic profile, etc.)); or a technical result manifested in the manufacture or use of the composition.

Annex 1

Table 7. List of registered ARV medicines in Kazakhstan[68]

№	Product licence number	Brand Name	Type	Date of Registr.	Manufacturer	ATC-code
1	RK-LS-5№020716	Abacavir and Lamivudine	Registration	27.11.2019	Aurobindo Pharma Limited	(J05AR02) Lamivudine and Abacavir
2	RK-LS-5№019939	Abacavir	Регистрация	19.09.2018	Милан Лаборатories Лимитед	(J05AF06) Абакавир
3	USP tablets	Registration	19.09.2018	Mylan Laboratories Limited	(J05AF06) Abacavir	(J05AR) Ламивудин/ Тенофовир/Эфавиренз 300 мг/300 мг/400 мг
4	RK-LS-5№023208	Avonza	Registration	05.09.2017	Mylan Laboratories Limited	(J05AR) Lamivudine/ Tenofovir/Efavirenz 300 mg/300 mg/400 mg
5	RK-LS-5№016561	Aluvia	Re-registration	25.09.2015	AbbVie Deutschland GmbH & Co	(J05AR10) Lopinavir and Ritonavir
6	RK-LS-5№014087	Aluvia	Re-registration	07.10.2019	AbbVie Deutschland GmbH & Co. КГ	(J05AR10) Lopinavir and Ritonavir
7	RK-LS-5№121752	Amiviren	Registration	23.10.2015	JSC "Pharmasyntez"	(J05AF05) Lamivudine
8	RK-LS-5№121751	Amiviren	Registration	23.10.2015	JSC "Pharmasyntez"	(J05AF05) Lamivudine
9	RK-LS-5№022492	Atazanavir and Ritonavir	Регистрация	16.02.2018	Абди Ибрахим Глобал Фарм	(J05AF06) Абакавир
10	RK-LS-5№005657	Registration	24.11.2016	Hetero Labs Limited	Combinations of antiviral drugs active against HIV	(J05AG01) Невирапин
11	RK-LS-3№021526	Virakar	Registration	16.02.2018	Abdi Ibrahim Global Pharm	(J05AF06) Abacavir
12	RK-LS-5№005657	Viramune	Re-registration	23.12.2016	West-Ward Columbus Inc.	(J05AG01) Nevirapine
13	RK-LS-5№020705	Viread	Re-registration	21.11.2019	Takeda GmbH	(J05AF07) Tenofovir disoproxil
14	RK-LS-5№015597	Virokomb	Re-registration	23.04.2015	Sun Pharmaceutical Industries Limited	(J05AR01) Zidovudine и Lamivudine
15	№ RK-LS-5№005491	Virol	Registration	14.08.2017	Sun Pharmaceutical Industries Limited	(J05AF06) Abacavir
16	RK-LS-5№016204	Virolam	Re-registration	25.09.2015	Sun Pharmaceutical Industries Limited	(J05AF05) Lamivudine
17	RK-LS-5№122110	Darunavir-AIGF	Registration	04.03.2016	Abdi Ibrahim Global Pharm	(J05AE10) Darunavir
18	RK-LS-5№122111	Darunavir-AIGF	Registration	04.03.2016	Abdi Ibrahim Global Pharm	(J05AE10) Darunavir
19	RK-LS-5№021638	Dizaverox	Registration	15.09.2015	JSC "Pharmasyntez"	(J05AR01) Zidovudine and Lamivudine
20	RK-LS-3№021498	Duolazid	Registration	23.04.2018	Abdi Ibrahim Global Pharm	(J05AR01) Zidovudine and Lamivudine
21	RK-LS-5№016700	Zeffix	Re-registration	19.11.2015	GlaxoSmithKline Inc.	(J05AF05) Lamivudine
22	RK-LS-5№003545	Zeffix	Re-registration	14.10.2015	GlaxoSmithKline Pharmaceuticals Ltd.	(J05AF05) Lamivudine
23	RK-LS-5№011980	Ziagen	Re-registration	29.01.2019	GlaxoSmithKline Pharmaceuticals Ltd.	(J05AF06) Abacavir
24	RK-LS-5№005698	Ziagen	Re-registration	02.12.2016	GlaxoSmithKline Inc.	(J05AF06) Abacavir
25	RK-LS-3№021549	Zidoas	Registration	15.06.2018	Abdi Ibrahim Global Pharm	(J05AF01) Zidovudine
26	RK-LS-5№021209	Intelence	Re-registration	13.02.2020	Janssen-Cilag Inc.	(J05AG04) Etravirine

[68]List of registered drugs for 29.05.2020. Available at: http://www.dari.kz/category/search_prep, https://drugs.medelement.com

№	Product licence number	Brand Name	Type	Date of Registr.	Manufacturer	ATC-code
27	RK-LS-5N№021157	Isentress	Registration	27.11.2019	Pateone Pharmaceuticals Inc.	(J05AX08) Raltegravir
28	RK-LS-5N№020768	Isentress	Registration	11.07.2019	MSD International GmbH / MSD Ireland (Ballidin)	(J05AX08) Raltegravir
29	RK-LS-5N№015503	Kaletra	Re-registration	18.05.2020	Aesica Queenborough Ltd.	(J05AR10) Lopinavir and Ritonavir
30	№ RK-LS-5N№122110	Kemeruvir	Registration	04.03.2016	JSC "Pharmasyntez"	(J05AE10) Darunavir
31	№ RK-LS-5N№122111	Kemeruvir	Registration	04.03.2016	JSC "Pharmasyntez"	(J05AE10) Darunavir
32	RK-LS-5N№005697	Kivexa	Re-registration	24.01.2017	Glaxo Operations UK ltd, Glaxo Wellcome Opeations	(J05AR02) Lamivudine and Abacavir
33	RK-LS-5N№010563	Combivir	Re-registration	23.10.2017	GlaxoSmithKline Pharmaceuticals Ltd.	(J05AR01) Zidovudine and Lamivudine
34	RK-LS-5N№022580	Complera	Registration	26.12.2016	Pateone Inc.	(J05AR08) Emtricitabine, Tenofovir disoproxil and Rilpivirine
35	RK-LS-3N№020658	Lamias 150	Re-registration	19.09.2017	Abdi Ibrahim Global Pharm	(J05AF05) Lamivudine
36	RK-LS-5N№023212	Lamivudine	Registration	06.09.2017	Strides Shasun Limited	(J05AF05) Lamivudine
37	RK-LS-5N№023000	Lamivudine and Zidovudine	Registration	25.05.2017	Strides Shasun Limited	(J05AR01) Zidovudine and Lamivudine
38	RK-LS-5N№121913	Lamivudine and Zidovudine	Registration	14.12.2015	Mylan Laboratories Limited	(J05AR01) Zidovudine and Lamivudine
39	№ RK-LS-5N№019229	Mivux	Registration	03.12.2019	NOBEL ALMATY PHARMACEUTICAL FACTORY	(J05AF05) Lamivudine
40	RK-LS-5N№016643	Nevipan	Re-registration	14.07.2016	Ranbaxy Laboratories Limited	(J05AG01) Nevirapine
41	№ RK-LS-5N№023603	Nevirapine	Registration	09.04.2018	Macleods Pharmaceuticals Ltd	(J05AG01) Nevirapine
42	RK-LS-5N№022943	Nevirapine	Registration	27.04.2017	Strides Shasun Limited	(J05AG01) Nevirapine
43	RK-LS-5N№021443	Nevirapine	Registration	25.06.2015	Aurobindo Pharma Limited	(J05AG01) Nevirapine
44	№ RK-LS-5N№021797	Nevirpine-AIGF	Registration	06.11.2015	Abdi Ibrahim Global Pharm	(J05AG01) Nevirapine
45	RK-LS-5N№017855	Norvir	Re-registration	21.02.2017	AbbVie Deutschland GmbH & Co. KГ	(J05AE03) Ritonavir
46	№ RK-LS-5N№024217	Odefsey	Registration	22.07.2019	Janssen-Cilag Inc.	J05AR19 (Emtricitabine, Tenofovir alafenamide and rilpivirine)
47	RK-LS-5N№121662	Olitide	Registration	14.10.2015	JSC "Pharmasyntez"	(J05AF06) Abacavir
48	RK-LS-5N№121663	Olitide	Registration	14.10.2015	JSC "Pharmasyntez"	(J05AF06) Abacavir
49	RK-LS-5N№019606	Prezista	Registration	14.11.2017	Janssen-Orto LLC	(J05AE10) Darunavir
50	RK-LS-5N№019607	Prezista	Registration	14.11.2017	Janssen-Orto LLC	(J05AE10) Darunavir
51	RK-LS-5N№121728	Regast	Registration	19.10.2015	JSC "Pharmasyntez"	(J05AG03) Efavirenz
52	RK-LS-5N№121729	Regast	Registration	19.10.2015	JSC "Pharmasyntez"	(J05AG03) Efavirenz
53	RK-LS-5N№022425	Rezolsta	Registration	13.10.2016	Janssen-Orto LLC	(J05AR14) Darunavir, Cobicistat
54	RK-LS-5N№011013	Retrovir	Re-registration	13.04.2018	GlaxoSmithKline Inc.	(J05AF01) Zidovudine

№	Product licence number	Brand Name	Type	Date of Registr.	Manufacturer	ATC-code
55	RK-LS-5N№011012	Retrovir	Re-registration	06.06.2018	GlaxoSmithKline Pharmaceuticals Ltd.	(J05AF01) Zidovudine
56	№ RK-LS-5N№024275	Symtuza	Registration	28.08.2019	Janssen-Cilag Inc..	(J05AR22) (Emtricitabine, Tenofovir alafenamide and, darunavir and cobicistat
57	RK-LS-5N№018110	Stokrin	Re-registration	30.06.2016	Zhejiang Huahai Pharmaceutical Co., Ltd.	(J05AG03) Efavirenz
58	№ РК-ЛС-5 №024575	Tavin	Registration	28.05.2020	Emcure Pharmaceuticals Ltd	(J05AF07) Tenofovir disoproxil
59	RK-LS-5N№019269	Telzir	Re-registration	07.09.2017	Glaxo Operations UK ltd, Glaxo Wellcome Opeations	(J05AE07) Fosamprenavir
60	RK-LS-5N№018506	Telzir	Re-registration	03.05.2017	GlaxoSmithKline Inc.	(J05AE07) Fosamprenavir
61	RK-LS-5N№020764	Tenofovir disoproxil Fumarate and Lamivudine	Registration	28.05.2020	Mylan Laboratories Limited	(J05AR12) Lamivudine, Tenofovira disoproxil
62	RK-LS-5N№020763	Tenofovir disoproxil Fumarate, Lamivudine and Efavirenz	Re-registration	28.05.2020	Mylan Laboratories Limited	(J05AR11) Lamivudine, Tenofovira disoproxil and Efavirenz
63	RK-LS-5N№021169	Tivicay	Re-registration	22.01.2020	Glaxo Operations UK ltd, Glaxo Wellcome Opeations	(J05AX12) Dolutegravir
64	RK-LS-5N№024007		Регистрация	29.01.2019	ВииВ Хэлзкеа Великобрита-ния Лимитед	J05AX12 Долутеграви р
65	RK-LS-5N№024008		ViiV Healthcare UK Limited	J05AX12 Dolutegravir	ВииВ Хэлзкеа Великобрита-ния Лимитед	J05AX12 Долутеграви р
66	RK-LS-5N№012399	Trizivir	Re-registration	01.11.2018	GlaxoSmithKline Pharmaceuticals Ltd.	(J05AR04) Zidovudine, Lamivudine and Abacavir
67	RK-LS-5N№022415	Triumeq	Registration	10.10.2016	Glaxo Operations UK ltd, Glaxo Wellcome Opeations	(J05AR13) Lamivudine, Abacavir and Dolutegravir
68	RK-LS-5N№022471	Edurant	Registration	15.11.2016	Janssen-Cilag Inc.	(J05AG05) Rilpivirine
69	№ RK-LS-5N№023521	Emtricitabine/ Tenofovir	Registration	09.02.2018	Strides Shasun Limited	(J05AF) Nucleosides - reverse transcriptase inhibitors
70	№ RK-LS-5N№023559	Emtricitabine/ Tenofovir - KPKA	Registration	02.03.2018	Krka, d. d	(J05AR03) Tenofovira disoproxil and Emtricitabine
71	RK-LS-5N№015500	Epivir	Re-registration	20.12.2019	GlaxoSmithKline Pharmaceuticals Ltd.	(J05AF05) Lamivudine
72	№ RK-LS-5N№023633	Efavirenz	Registration	04.05.2018	Macleods Pharmaceuticals Ltd	(J05AG03) Efavirenz
73	№ RK-LS-5N№020048	Efavirenz USP	Re registration	14.06.2019	Mylan Laboratories Limited	(J05AG03) Efavirenz
74	RK-LS-5N№020725	Efavirenz, Emtricitabine and Tenofovir disoproxil Fumarate	Registration	16.10.2019	Aurobindo Pharma Limited	(J05AR06) Emtricitabine, Tenofovir Disoproxil and Efavirenz
75	№ RK-LS-5N№023679	Efavirenz/ Emtricitabine/ Tenofovir	Registration	31.05.2018	Strides Shasun Limited	(J05AR06) Emtricitabine, Tenofovir disoproxil and Efavirenz

№	Product licence number	Brand Name	Type	Date of Registr.	Manufacturer	ATC-code
76	№ RK-LS-5№121729	Efavirenz-AIGF	Registration	19.10.2015	Abdi Ibrahim Global Pharm	(J05AG03) Efavirenz
78	RK-LS-5№024219	Efavirenz/ Emtricitabine/ Tenofovir - KRKA	Registration	23.07.2019	KRKA,d.d.,Novo Mesto	J05AR03 Tenofovir disoproxil and Emtricitabine
79	№ 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 2019

INN	Drug dosage form	Brand Name	Pre-packing	Quantity, unit	Number of Packs	Supplier
Abacavir	Coated tablets, 300 mg	Virakar®	60	6420	107	Abdi Ibrahim Global Pharm
Zidovudine	Capsules, 100 mg	Zidoas	60	17800	296,6	Abdi Ibrahim Global Pharm
Zidovudine+ Lamivudine	Coated tablets, 300 mg/150 mg	Duolazide	60	1003200	16720	Abdi Ibrahim Global Pharm
Lamivudine	tablet, 150 mg	Lamias® 150	60	36600	610	Abdi Ibrahim Global Pharm
Abacavir	Oral solution, 20 mg/ml 240 ml	Ziagen®	1	1065	1065	GlaxoSmithKline Inc..
Abacavir+ Lamivudine+ Zidovudine	Film-coated tablets 300mg/150mg/300mg	Trizivir®	60	56280	938	GlaxoSmithKline Pharmaceuticals S.A.,
Darunavir + Cobicistat	Film-coated tablets 800 mg/150 mg	Rezolsta®	30	250830	8361	Janssen – Orto LLC,
Dolutegravir	Film-coated tablets, 50 mg	Tivikay®	30	37260	1242	Glaxo Operations UK ltd.
Dolutegravir	Tablet, 50 mg	Tivikay®	30	658290	21943	Glaxo Operations UK ltd.
Zidovudine	Oral solution, 10 mg/ml 200 ml	Retrovir	1	2727	2727	GlaxoSmithKline Inc.., Canada, an owner RU ViiV Healthcare, Canada
Lamivudine	Oral solution, 5 mg/ml 240 ml	Zeffix®	1	3875	3875	GlaxoSmithKline Inc..,
Lamivudine + Abacavir + Dolutegravir	Film-coated tablets, 300 mg/600 mg/50 mg	Triumeq®	30	174720	5824	Glaxo Operations UK ltd.
Emtricitabine+ Tenofovir+ Rilpivirine	Film-coated tablets	Komplera	30	96240	3208	Janssen-Cilag Inc.
Etravirine	Tablets 100 mg	Intelence®	120	8280	69	Janssen-Cilag Inc.
Etravirine	Tablets 200 mg	Intelence®	60	65520	1092	Janssen-Cilag Inc.
Etravirine	Tablets 200 mg	Intelence®	60	94020	1567	Janssen-Cilag Inc.
Lopinavir + Ritonavir	Film-coated tablets, 100 mg/25 mg	Aluvia	60	141360	2356	AbbVie Deutschland GmbH & Co.
Lopinavir + Ritonavir	Film-coated tablets, 200 mg/50 mg	Aluvia	120	1672800	13940	AbbVie Deutschland GmbH & Co.
Lopinavir + Ritonavir	Film-coated tablets, 200 mg/50 mg	Aluvia	120	393120	3276	AbbVie Deutschland GmbH & Co.
Lopinavir + Ritonavir	Oral solution, 60 ml	Kaletra®	5	1110	222	AbbVie Deutschland GmbH & Co.
Nevirapine	Tablets, 200 mg	Viramune®	60	46800	780	Boehringer Ingelheim Ellas, A.E.
Nevirapine	Oral suspension, 50 mg/5 ml 240 ml	Viramune®	1	2233	2233	Boehringer Ingelheim GmbH
Abacavir	Tablet, 300 mg	Ziagen®	60	58860	981	GlaxoSmithKline Pharmaceuticals S.A.,

INN	Drug dosage form	Brand Name	Pre-packing	Quantity, unit	Number of Packs	Supplier
Abacavir+ Lamivudine	Tablet, 600 mg/300mg	Kivexa®	30	53160	1772	GlaxoSmithKline Pharmaceuticals S.A.
Abacavir+ Lamivudine	Tablet, 600 mg/300mg	Kivexa®	30	921210	30707	GlaxoSmithKline Pharmaceuticals S.A.
Zidovudine	Capsules, 100 mg	Retrovir®	100	44700	447	GlaxoSmithKline Pharmaceuticals S.A.
Zidovudine+ Lamivudine	Tablet, 300 mg/150 mg	Combivir	60	134100	2235	GlaxoSmithKline Pharmaceuticals S.A.
Lamivudine	Tablet, 150 mg	Epivir®	60	56580	943	GlaxoSmithKline Pharmaceuticals S.A.
Nevirapine	tablet, 200 mg	Nevivir	60	88200	1470	HETERO LABS LIMITED , India
Tenofovir+ Emtricitabine+ Efavirenz	Tablet, 300 mg/200 mg/600 mg	Efavirenz, Emtricitabine, Tenofovira Disoproxil Fumarate	30	2468970	82299	Hetero Labs Limited , India
Tenofovir	Film-coated tablets 300mg	Tenofovira Disoproxil Fumarate	30	922140	30738	Mylan Laboratories Limited
Emtricitabine+ Tenofovir	Tablet, 200 mg/300 mg	Tenochop-e	30	1321710	44057	Macleods Pharmaceuticals Ltd.
Efavirenz	Tablet, 600 mg	Efavirenz	30	466020	15534	Hetero Labs Limited
Efavirenz	Tablet/Capsules, 200 mg	Efavirenz	90	154800	1720	Strides Shasun Limited
Emtricitabine+ Tenofovir	Tablet, 200 mg/300 mg	Truvada	30	17910	597	Takeda GmbH
Efavirenz	Tablet/Capsules, 200 mg	Stocrin®	90	128430	1427	Zhejiang Huahai Pharmaceutical Co., Ltd.
Etravirine	Tablets 200 mg	Intelence®	60	95460	1591	Janssen Pharmaceutica NB
Etravirine	Tablets 100 mg	Intelence®	120	124080	1034	Janssen Pharmaceutica NB
Etravirine	Tablets 200 mg	Intelence®	60	6300	105	Janssen Pharmaceutica NB
Efavirenz	Tablet, 600 mg	Efavirenz	30	644370	21479	UNICEF, United Nations Children's Fund
Efavirenz	Coated tablets, 200mg	Stocrin®	90	69300	770	AK NIET, LTD
Efavirenz	Tablet, 200 mg	Efavirenz	90	55710	619	UNICEF, United Nations Children's Fund

Annex 3.

Table 3. Cost of Each Medicine in the Total Budget

INN	Brand Name	Manufacturer	Number of units	Supplier's cost, KZT	Supplier's cost, USD [69]
Abacavir, tablet 300mg	Virakar®	Abdi Ibrahim Global Pharm, LLP	6420	3 558 028,20	9 295,96
Zidovudine, capsule 100mg	Zidoas	Abdi Ibrahim Global Pharm, LLP	17800	1 889 470,00	4 936,56
Zidovudine+ Lamivudine, tablets 300 mg/150 mg	Duolazide	Abdi Ibrahim Global Pharm, LLP	1003200	280 785 648,00	733 600,65
Lamivudine, tablet 150 mg	Lamias® 150	Abdi Ibrahim Global Pharm, LLP	36600	14 866 188,00	38 840,47
Abacavir,solution 20 mg/ml 240 ml	Ziagen®	GlaxoSmithKline Inc.	1065		
Abacavir+ Lamivudine+ Zidovudine, 300mg/150mg/300mg	Trizivir®	GlaxoSmithKline Pharmaceuticals S.A.	56280		
Darunavir + Cobicistat, 800 mg/150 mg	Rezolsta®	Janssen – Orto LLC	250830		
Dolutegravir, 50 mg	Tivicay®	Glaxo Operations UK ltd.	37260		
Dolutegravir, 50 mg	Tivicay®	Glaxo Operations UK ltd.	658290		
Zidovudine, solution 10 mg/ml, 200 ml	Retrovir	GlaxoSmithKline Inc., Canada, RU ViiV Healthcare, Canada	2727		
Lamivudine, solution 5mg/ml 240 ml	Zeffix®	GlaxoSmithKline Inc.	3875		
Lamivudine + Abacavir + Dolutegravir, 300 mg/600 mg/50 mg	Triumeq®	Glaxo Operations UK ltd	174720		
Emtricitabine+ Tenofovir + Rilpivirine,	Complera	Janssen-Cilag Inc.	96240		
Etravirine, 100 mg	Intelens®	Janssen-Cilag Inc.	8280		
Etravirine, 200 mg	Intelens®	Janssen-Cilag Inc.	65520		
Etravirine, 200 mg	Intelens®	Janssen-Cilag Inc.	94020		
Lopinavir+ Ritonavir, 100 mg/25 mg	Aluvia	AbbVie Deutschland GmbH & Co.	141360	8 450 500,80	22 078,38
Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	AbbVie Deutschland GmbH & Co.	1672800	290 682 456,00	759 457,76

[69] 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
Lopinavir+ Ritonavir, 200 mg/50 mg	Aluvia	AbbVie Deutschland GmbH & Co.	393120	68 312 462,40	178 478,02
Lopinavir+ Ritonavir, 60 ml	Kaletra®	AbbVie Deutschland GmbH & Co.	1110	3 546 572,10	9 266,03
Nevirapine, 200 mg	Viramune®	Boehringer Ingelheim Ellas A.E.	46800	6 758 856,00	17 658,67
Nevirapine, 50 mg/5 ml 240 ml	Viramune®	Boehringer Ingelheim GmbH	2233	7 450 426,83	19 465,52
Abacavir, 300 mg	Ziagen®	GlaxoSmithKline Pharmaceuticals S.A.	58860		
Abacavir+ Lamivudine	Kivexa®	GlaxoSmithKline Pharmaceuticals S.A.	53160		
Abacavir+ Lamivudine	Kivexa®	GlaxoSmithKline Pharmaceuticals S.A.	921210		
Zidovudine, 100 mg	Retrovir	GlaxoSmithKline Pharmaceuticals S.A.	44700		
Zidovudine+ Lamivudine	Combivir	GlaxoSmithKline Pharmaceuticals S.A.	134100		
Lamivudine, 150 mg	Epivir®	GlaxoSmithKline Pharmaceuticals S.A.	56580		
Nevirapine, 200 mg	Nevivir	Hetero Labs Limited	88200		
Tenofovir+ Emtricitabine+ Efavirenz	Efavirenz, Emtricitabine, Tenofovir Disoproxil Fumarate	Hetero Labs Limited	2468970		
Tenofovir, 300 mg	Tenofovir Disoproxil Fumarate	Mylan Laboratories Limited	922140		
Emtricitabine+ Tenofovir	Tenochop-e	Macleods Pharmaceuticals Lmt.	1321710		
Efavirenz, 600mg	Efavirenz	Hetero Labs Limited	466020		
Etravirine, 200 mg	Efavirenz	Strides Shasun Limited	154800		
Emtricitabine+ Tenofovir	Truvada	Takeda GmbH	17910		
Efavirenz	Stocrin®	Zhejiang Huahai Pharmaceutical Co., Ltd.	128430		
TOTAL				**686 300 608,33**	**1 793 078,02**

Annex 4

Table 4. Actual Prices and Contract Amounts for ARV Drugs Purchased in 2019.

INN	Brand Name	Drug dosage form	Manufac-turer	Supplier's cost per unit, KZT	Supplier's cost per package, KZT	Cost per patient per year, KZT	Cost per patient per year, USD[70]	Total amount, Supplier's price
Abacavir, tablet 300 mg	Virakar®	60	Abdi Ibrahim Global Pharm, LLP	554,21	33 252,60	404 573,30	1 057,02	3 558 028,20
Zidovudine, capsule 100mg	Zidoas	100	Abdi Ibrahim Global Pharm, LLP	106,15	10 615,00	232 468,50	607,36	1 889 470,00
Zidovudine+ Lamivudine, tablets 300 mg/150 mg	Duolazide	60	Abdi Ibrahim Global Pharm, LLP	279,89	16 793,40	204 319,70	533,82	280 785 648,00
Lamivudine, tablet, 150 mg	Lamias® 150	60	Abdi Ibrahim Global Pharm, LLP	406,18	24 370,80	296 511,40	774,69	14 866 188,00
Lopinavir + Ritonavir, 100 mg/25 mg	Aluvia	60	AbbVie Deutschland GmbH & Co.	59,78	3 586,80	0,00	0,00	8 450 500,80
Lopinavir + Ritonavir, 200 mg/50 mg	Aluvia	120	AbbVie Deutschland GmbH & Co.	173,77	20 852,40	253 704,20	662,85	290 682 456,00
Lopinavir + Ritonavir, 200 mg/50 mg	Aluvia	120	AbbVie Deutschland GmbH & Co.	173,77	20 852,40	253 704,20	662,85	68 312 462,40
Lopinavir + Ritonavir, 60 ml	Kaletra®	1	AbbVie Biopharma-ceuticals GmbH.	3 195,11	3 195,11	0,00	0,00	3 546 572,10
Nevirapine, 200 mg	Viramune®	60	Boehringer Ingelheim Ellas A.E.	144,42	8 665,20	105 426,60	275,45	6 758 856,00
Nevirapine, 50 mg/5 ml 240 ml	Viramune®	1	Boehringer Ingelheim GmbH	3 336,51	3 336,51	0,00	0,00	7 450 426,83
TOTAL								686 300 608,33

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

Annex 5

Table 5. Estimated Number of Annual Regimens per an ARV Drug

INN	Brand Name	Drug dosage form	Manufac-turer	Dosing schedule (number of tablets per day)	Number of units	Estimated number of annual treatment courses	Category of patients [71]
Abacavir, tablet 300 mg	Virakar®	60	Abdi Ibrahim Global Pharm, LLP	2	6420	8,79	Adults
Zidovudine, capsule 100mg	Zidoas	100	Abdi Ibrahim Global Pharm, LLP	6	17800	8,13	Children
Zidovudine+ Lamivudine, tablets 300 mg/150 mg	Duolazide	60	Abdi Ibrahim Global Pharm, LLP	2	1003200	1 374,25	Adults
Lamivudine, tablet, 150 mg	Lamias® 150	60	Abdi Ibrahim Global Pharm, LLP	2	36600	50,14	Adults
Abacavir, solution 20 mg/ml 240 ml	Ziagen®	1	GlaxoSmith Kline Inc..	0	1065	0,00	Children
Abacavir+ Lamivudine+ Zidovudine, 300mg/150mg/300mg	Trizivir®	60	GlaxoSmith Kline Pharmaceuticals S.A.,	2	56280	77,10	Adults
Darunavir + Cobicistat, 800 mg/150 mg	Rezolsta®	30	Janssen – Orto LLC,	1	250830	687,21	Adults
Dolutegravir, 50 mg	Tivicay®	30	Glaxo Operations UK ltd.	1	37260	102,08	Adults
Dolutegravir, 50 mg	Tivicay®	30	Glaxo Operations UK ltd..	1	658290	1 803,53	Adults
Zidovudine, solution 10 mg/ml 200 ml	Retrovir	1	GlaxoSmithKline Inc.., Canada	0	2727	0,00	Children
Lamivudine, solution 5 mg/ml 240 ml	Zeffix®	1	GlaxoSmithKline Inc..	0	3875	0,00	Children
Lamivudine + Abacavir + Dolutegravir, 300 mg/600 mg/50 mg	Triumeq®	30	Glaxo Operations UK ltd..	1	174720	478,68	Adults
Emtricitabine + Tenofovir+ Rilpivirine	Complera	30	Janssen-Cilag S A,	1	96240	263,67	Adults
Etravirine, 100 mg	Intelens®	120	Janssen-Cilag S A,	4	8280	5,67	Adults
Etravirine, 200 mg	Intelens®	60	Janssen-Cilag S A,	2	65520	89,75	Adults
Etravirine, 200 mg	Intelens®	60	Janssen-Cilag S A	2	94020	128,79	Adults
Lopinavir + Ritonavir, 100 mg/25 mg	Aluvia	60	AbbVie Deutschland GmbH & Co.	0	141360	0,00	Children
Lopinavir + Ritonavir, 200 mg/50 mg	Aluvia	120	AbbVie Deutschland GmbH & Co.	2	1672800	2291,51	Adults
Lopinavir + Ritonavir, 200 mg/50 mg	Aluvia	120	AbbVie Deutschland GmbH & Co	2	393120	538,52	Adults
Lopinavir + Ritonavir, 60 ml	Kaletra®	1	AbbVie Biopharma-ceuticals GmbH.	0	1110	0,00	Children

[71] The calculation for children was not carried out as there are no exact data on the ages of the children

INN	Brand Name	Drug dosage form	Manufac-turer	Dosing schedule (number of tablets per day)	Number of units	Estimated number of annual treatment courses	Category of patients
Nevirapine, 200 mg	Viramune®	60	Boehringer Ingelheim Ellas A.E.,	2	46800	0,00	Children
Nevirapine, 50 mg/5 ml 240 ml	Viramune®	1	Boehringer Ingelheim GmbH	0	2233	0,00	Children
Abacavir, 300 mg	Ziagen®	60	GlaxoSmith Kline Pharmaceuticals S.A.,	2	58860	80,63	Adults
Abacavir+ Lamivudine	Kivexa®	30	GlaxoSmithKline Pharmaceuticals S.A.	1	53160	145,64	Adults
Abacavir+ Lamivudine	Kivexa®	30	GlaxoSmithKline Pharmaceuticals S.A.	1	921210	2 523,86	Adults
Zidovudine, capsule, 100 mg	Retrovir®	100	GlaxoSmithKline Pharmaceuticals S.A.	6	44700	0,00	Children
Zidovudine+ Lamivudine	Combivir	60	GlaxoSmithKline Pharmaceuticals S.A.	2	134100	0,00	Children
Lamivudine, 150 mg	Epivir®	60	GlaxoSmithKline Pharmaceuticals S.A.	2	56580	0,00	Children
Nevirapine, 200 mg	Nevivir	60	Hetero Labs Limited	2	88200	120,82	Adults
Tenofovir+ Emtricitabine + Efavirenz	Efavirenz, tricitabine, Tenofovir Disoproxil Fumarate	30	Hetero Labs Limited	1	2468970	6 764,30	Adults
Tenofovir, 300mg	Tenofovir Disoproxil Fumarate	30	Mylan Laboratories Limited	1	922140	2 526,41	Adults
Emtricitabine + Tenofovir	Tenochop-e	30	Macleods Pharmaceuticals Lmt.	1	1321710	3 621,12	Adults
Efavirenz, 600 mg	Efavirenz	30	Hetero Labs Limited	1	466020	1 276,77	Adults
Efavirenz, 200 mg	Efavirenz	90	Strides Shasun Limited	2	154800	212,05	Adults
Emtricitabine +Tenofovir	Truvada	30	Takeda GmbH	1	17910	0,00	Children
Efavirenz, 200 mg	Stocrin®	90	Zhejiang Huahai Pharmaceutical Co., Ltd	1	128430	0,00	Children

Annex 6

Table 6. List of the registered HCV medicines in Kazakhstan

№	Product licence number	International non-proprietory name (INN)	Brand name	Type of action	Marketing start date (dd/mm/yy)	Manufac-turer	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№022268/ 69	Pegylated interferon alpha-2b	Pegaltivir	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	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	Абди Ибрахим Глобал Фарм	36,90	J05AB04
10	RK-LS 5№005086	Ribavirin	REBETOL	Re-registration	21.02.2017	MSD International GmbH (Puerto Rico Branch) LLC	32134 ,33	J05AB04
11	RK-LS 5№022490	Sofosbuvir	SOFGEN	Registration	24.11.2016	Hetero Labs Limited.	35270. 02	J05AX15
12	RK-LS 5№023213	Sofosbuvir	VIRSO	Registration	07.09.2017	Strides Shasun Limited	83499, 00	J05AX15
13	RK-LS 5№022703	Sofosbuvir	GRATEZIANO	Registration	20.01.2017	European Egyptian Pharmaceuticals Ind	Нет	J05AX15
14	RK-LS-5№024005	Sofosbuvir	VALDIS	Registration	24.01.2019	SHROOQ PHARMA-CEUTICAL (Pvt.) Ltd.	62961, 03	J05AX15
15	RK-LS-5№024077	Sofosbuvir	NUCLEO-BUVIR	Registration	18.04.2019	Eva Pharma for pharmaceuticals and medical appliances S.A.E.	Нет	J05AX15
16	RK-LS 5№023276	Daclatasvir	VIRDAK	Registration	03.10.2017	Hetero Labs Limited.	24317, 00	J05AX14
17	RK-LS 5№024005	Sofosbuvir	VALDIS	Registration	10.04.2019	Eva Pharma for pharmaceuticals and medical appliances S.A.E.	Нет	J05AX14