BRACE
Law Firm

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DIGEST
of regulation of the Russian pharmaceutical industry

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Dear Colleagues!

We are glad to propose to you the next digest of regulation of the Russian pharmaceutical industry for March 2019, prepared by BRACE Law Firm.

The previous month, the Board of the Eurasian Economic Commission approved important Recommendations relating to the actualization of notions used within the framework of the Eurasian Economic Union in the field of medicine circulation, given in the relevant information directory, as well as the procedure for requesting drugs.

At the level of federal legislation, a step forward has been made regarding the clarification of a number of issues related to the legal regulation of the provision of palliative care.

The Ministry of Healthcare ruled to cancel the state registration of drugs that have not been in circulation for three and more years.

March of 2019 was rather active in lawmaking. In particular, legislative initiatives have been made to toughen liability for non-compliance with licensing requirements in the production of medicines, and it is proposed to approve the procedure for monitoring movement and accounting of medicines intended to provide individuals suffering from serious illnesses such as hemophilia, cystic fibrosis, pituitary ganosis, Gaucher disease, malignant neoplasms.

Noteworthy that according to the practice of the Federal Antimonopoly Service of Russia similar names of biologically active food supplements and medicines are qualified as misleading.

Sincerely yours,

BRACE Law Firm

1. Laws, by-laws, legal news

1.1. The Board of the Eurasian Economic Commission approved the Recommendation on the updated Information Handbook of the concepts used within the framework of the Eurasian Economic Union in the field of drug circulation.

Recommendation of the Board of the Eurasian Economic Commission dated March 19, 2019 N 10 "On the updated Information Handbook of the concepts used in the framework of the Eurasian Economic Union in the field of circulation of medicines"

According to the Agreement on Common Principles and Rules for the Circulation of Medicinal Products within the Eurasian Economic Union (hereinafter referred to as the EEU), concluded in Moscow on December 23, 2014, the EEU member states should be guided by the unified notions established by the reference book of concepts and definitions in the field of drug circulation.

The updated information directory contains a number of new notions and definitions to them. For example, such as:

- Biobatch – series used in a clinical study of bioavailability (bioequivalence) or a clinical efficacy study (confirming the presence of the functional characteristics of the dosage form). The size of the bioseriy corresponds to at least the size of the pilot industrial series, that is, for solid dosage forms for oral administration, it is at least 10% of the series size with full-scale production or 100,000 units of the dosage form (depending on which of these indicators is larger)
- Process Validation – documented confirmation that the manufacturing process, performed within the established parameters, effectively and reproducibly ensures the production of a drug that meets predetermined specifications and quality indicators.
- Expiration Date (Shelf Life) – the date indicated on the labeling of the container of a pharmaceutical substance or drug and indicating the end of the period during which (inclusive) when stored under specified conditions, they will meet the approved specifications and after which they cannot be used.
- Dumping dose (dose reset) – unintentionally quick release of the active substance from the dosage form.

We believe that the actualization of this Information Guide is reasonable and more consistent with practical needs the harmonization of terminology used by the EEU member states.

1.2. The Board of the Eurasian Economic Commission made recommendations on the selection of the dose of drugs.

Recommendation of the Board of the Eurasian Economic Commission dated March 12, 2019 N 8 «On the Guidelines for the selection of the dose of drugs»

This document, which comes into force on September 15, 2019, establishes that when registering drugs in order to reduce cases of registration with an indication of excessive dosing regimen, when studying them, the smallest dose that has a clear positive effect, or the maximum dose that does not lead to additional increase in the desired positive effect. The most valuable choice of starting dose is the knowledge of the shape and location of the population average dose-effect curve for desired effects and undesirable reactions. In determining the dose-effect relationship, diagnostic and therapeutic approaches should be taken into account that affect the standardized types of research in each of the clinical areas.

The choice of design in dose-effect studies is determined by the phase of drug development, the studied indications for use and the severity of the disease in the target group of patients. For

example, the lack of necessary therapy in life-threatening or serious pathological conditions with an irreversible outcome may, for ethical reasons, prevent the conduct of research in doses below the maximum tolerated. In this case, the document presents various designs of clinical studies that have proven to be effective in the study of the dose-effect relationship, as well as general guidelines for research designs.

1.3. Additional legal for medical intervention without consent of the patient, his parents or legal representatives.

Federal Law of March 06, 2019 N 18-ФЗ «On Amendments to the Federal Law» On the Basics of Health Protection of Citizens in the Russian Federation «on the provision of palliative medical care»

Now the decision on medical intervention without the consent of a citizen, one of the parents or another legal representative can be taken regarding provision of palliative medical care if the state of a patient does not allow him to express his will and there is no legal representative. Such a decision is made by the medical commission, and if it is impossible to collect the medical commission, a consultation of doctors or the attending physician (on duty) with this decision in the patient's medical documentation and the subsequent mandatory notification of the management of the medical organization, one of whom parents or other legal representative.

The concept of "palliative care" is defined as a set of measures, including medical interventions, psychological measures and care, carried out in order to improve the quality of life of incurable patients and aimed at alleviating pain and other severe manifestations of the disease.

Palliative medical care is provided on an outpatient basis, including at home, and in a day hospital, inpatient setting. To provide palliative care, medical professionals must undergo special training.

1.4. The obligation to cancel the state registration of drugs that have not been in circulation for three and more years.

Letter N 20-3 / 328 of March 4, 2019 of the Ministry of Health of the Russian Federation "On the submission to the Ministry of Health of Russia of an application on the cancellation of state registration of drugs that are not in circulation in the territory of the Russian Federation for three years or more"

It establishes the obligation of the holder or owner of the registration certificate of a medicinal product or an application authorized by another legal entity when submitting an application for cancellation of the state registration of a medicinal product that has not been in circulation in the Russian Federation for three or more years.

1.5. The Government has made changes to the state program for the development of the pharmaceutical and medical industry.

Resolution of the Government of the Russian Federation dated March 29, 2019 N 359 "On Amendments to the Resolution of the Government of the Russian Federation" dated April 15, 2016 N 305

The main directions of development of the pharmaceutical and medical industry are invited to include:

- transition to the path of innovative development;
- changes in the structure and scale of production of medicines and medical devices;
- creating a competitive market environment;

- integration into the global system of production and consumption of medicines and medical devices.

Changes are made to such indicators as the share of locally produced medicines (53%) and medical devices (43%) of the total consumption in monetary terms.

In addition, the main objectives of the Program include the formation of the scientific, technological and production potential of the pharmaceutical industry.

1.6. Identified signs of falsification of the drug "Vidaza".

Letter of Roszdravnadzor dated March 26, 2019 N 01I-798/19 "On signs of falsification of the drug Vidaza"

This letter lists signs of falsification of the drug Vidaza, a lyophilisate for the preparation of suspensions for subcutaneous administration of 100 mg, vials (1), packs of cardboard 7B965A series, suggesting the implementation of testing by medical organizations procuring the drug for the presence / absence of signs of falsification.

2. Drafts of legal acts

2.1. The Ministry of Health has submitted for public discussion the question of preparing a draft of changes in the standards for calculating the need for narcotic and psychotropic medicinal substances.

Draft Order of the Ministry of Health of the Russian Federation "On Amendments to the Order of the Ministry of Health of the Russian Federation dated December 01, 2016 N 917n "On approval of standards for calculating the need for narcotic and psychotropic medicines intended for medical use"

It is explained that this project is planned to be prepared in order to calculate the need for the formation of stocks of narcotic and psychotropic medicines intended for medical use, depending on the number of patients requiring them, as well as the need to provide patients with narcotic and psychotropic medicines at home.

Currently, standards are calculated per 1,000 people per year without setting standards separately for home care. We believe that the need for the preparation of such a project is relevant now and will allow to obtain more accurate calculations of the need for these medicines.

2.2. The Ministry of Health of Russia proposes to declare the requirements of narcotic drugs annually invalid.

Draft Order of the Ministry of Health of Russia "On recognition of annex 3 to the order of the Ministry of Health of the Russian Federation of 12 November 1997 N 330 "On measures to improve the accounting, storage, discharge and use of narcotic drugs and psychotropic substances" and the order of the Ministry of Health of the Russian Federation of January 9, 2001 N 2 "On Amendments and Addenda to the Order of the Ministry of Health of Russia of 12 November 1997 N 330 "On measures to improve the accounting, storage, discharge and use of drugs medicines"

This draft document recognizes the estimated requirements of narcotic drugs and psychotropic substances per 1000 people of the population per year (in grams), as well as the norms of the previously adopted order of the Ministry of Health of the Russian Federation, amending the relevant annex, which specifies these standards.

2.3. The Ministry of Health has been asked to approve the rules for reregistering the marginal prices for vital and essential medicines.

Draft Resolution of the Government of the Russian Federation "On Approval of the Rules for Mandatory Re-Registration in 2019–2020 of the Registered Manufacturers' Limit Prices for Medicinal Products Included in the List of vital and essential medicinal products and amendments to certain acts of the Government of the Russian Federation in regarding state registration and re-registration marginal selling prices for drugs included in the list of vital and essential medicines medications"

The draft resolution establishes the rules for mandatory re-registration in 2019-2020 of all previously registered by various methods before the bill enters into force, the maximum selling prices for drugs included in the list of vital and essential drugs (hereinafter - the VED list).

From January 1, 2021, manufacturers are not allowed to sell drugs on which the maximum selling prices are not reregistered.

2.4. The Ministry of Health of Russia proposes to change the timing of the use of reference prices when calculating the initial (maximum) contract price when purchasing medicines.

Draft Order of the Ministry of Health of the Russian Federation "On Amendments to the procedure for determining the Initial (maximum) contract price, contract price, concluded with a single supplier (contractor, performer) when purchasing medicines for medical use, approved by order of the Ministry of Health of the Russian Federation dated 26 October 2017 N 871n"

It is proposed to establish that the application of reference prices by customers is carried out if the relevant information is posted in the Unified Information System.

This change is due to the fact that, in accordance with the implementation of the plan of measures to determine the interchangeability of drugs, their interchangeability will be determined between groups of drugs combined according to the principle of equality of the values of international non-proprietary names, dosage forms and dosages. At the same time, a phased transition to the calculation of reference prices for medicines during 2019 is planned.

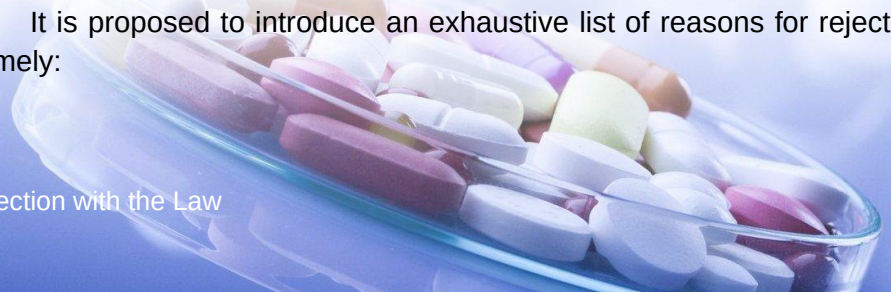
2.5. The Ministry of Health of Russia proposes to approve the procedure for monitoring movement and accounting of drugs for patients with hemophilia, cystic fibrosis, pituitary nanism, Gaucher disease, and malignant neoplasms.

Draft Order of the Ministry of Health of Russia "On approving the procedure for monitoring movement and accounting of drugs in the subjects of the Russian Federation intended to provide persons with hemophilia, cystic fibrosis, pituitary nanism, Gaucher disease, lymphoid lymphoid neoplasms, related to them, multiple sclerosis, hemolytic -uremic syndrome, juvenile arthritis with systemic onset, mucopolysaccharidosis type I, II and VI, after organ and/or tissue transplantation, individuals Denia to the authorized bodies of executive power of the Russian Federation received the results of the monitoring data and matching applications authorized by the executive authorities of the Russian Federation on the redistribution of drugs among the subjects of the Russian Federation"

It is proposed to impose on the Department of drug provision and regulation of the circulation of medical devices of the Ministry of Health of Russia responsibilities for the organizational support of the monitoring of relevant drugs.

It is specified that information is submitted to the Department for review about drugs that are analyzed and sent by the Department to the authorized bodies. In turn, the authorized bodies consider summarized data on drugs submitted by the Department and send an application to the Department for consideration and approval on the redistribution of drugs.

It is proposed to introduce an exhaustive list of reasons for rejecting the submitted application. Namely:



- determination of the absence of need for the declared medicinal preparations according to the results of the monitoring;
- indication in the application of the name and (or) dosage form, and (or) dosage of the medicinal product for which redistribution is not carried out.

2.6. The Ministry of Industry and Trade of Russia proposes to toughen the responsibility for non-compliance with licensing requirements in the production of medicines, as well as for non-compliance with the requirements and instructions of the bodies exercising licensing control.

Draft federal law "On Amendments to the Code of the Russian Federation on Administrative Offenses"

The draft law provides for amendments to the Code of Administrative Offenses of the Russian Federation, to increase responsibility for violations of licensing requirements in the production of medicines as well as for non-compliance with legal requirements, non-compliance with the statutory instructions of an official of the federal executive body exercising licensing control (supervision) in the production of medicines for medical use, as well as preventing them from executive duties.

Namely, for non-compliance with the requirements of the authorized control (supervisory) body, it is proposed to introduce responsibility in the form of the imposition of an administrative fine on officials in the amount of from 5000 to 10000 rubles; for legal entities - from 50000 to 500000 rubles or suspension of the license. Repeated within 3 years, the commission of this administrative offense may entail the imposition of an administrative fine on officials in the amount of from 30000 to 40000 rubles; on legal entities - from 100000 to 1000000 rubles, or suspension of a license.

For the production of medicines for medical use with a gross violation of the requirements and conditions stipulated by the license, a measure of responsibility is proposed in the form of imposing an administrative fine on officials - from 100000 to 200000 rubles; for legal entities - from 1000000 to 50000000 rubles, or suspension of a license.

2.7. The Ministry of Industry and Trade of Russia proposed to supplement the Procedure for suspending, renewing and revoking a license to carry out drug production activities.

Draft federal law "On Amendments to Article 1 of the Federal Law "On licensing certain types of activities" and Federal Law "On the circulation of medicines"

The draft law is aimed at bringing the current legislation in accordance with the requirements of the Agreement on common principles and rules for the circulation of medicines within the EEU in order to pursue a coordinated policy on the circulation of medicines and the general requirements for regulating the circulation of medicines, including their production from December 23, 2014.

It is proposed to establish that the license is suspended by the licensing authority for a period until the elimination of the causes, but not more than 3 years in the following cases:

1) non-fulfillment in the prescribed period of the prescription of the licensing authority to eliminate the identified violation;

2) re-committing the same violation within 3 years;

3) detection of the fact of production of drugs that are not included in the state register of drugs;

4) obstruction of the legal activities of an official of the licensing authority for conducting inspections;

5) the absence of the licensee at the place of the licensed type of activity;

6) detecting during the verification of the absence of premises and (or) equipment at the place of implementation of the production of medicines;

7) detection by the licensing body of gross violation of licensing requirements;

8) submission by another state control (supervision) body, which, within its competence, carries out control measures, information on the facts of a threat of causing and harm to life and health of citizens.

According to the draft law, the license is canceled by the court decision on the basis of consideration of the application of the licensing authority to revoke a license in the following cases:

1) repeated commission within one year (from the moment of the previous violation) of a gross violation by the licensee of licensing requirements;

2) non-elimination by the licensee within the time period specified by the licensing authority for the violation that resulted in the suspension of the license.

3. Judicial and law enforcement practice

3.1. The Russian Federal Antimonopoly Service justifies the reasons for high drug prices.

Presentation by the Head of the Drug Price Regulation Department of the Social and Trade Control Department of the Federal Antimonopoly Service of Russia Darya Starykh on the role of indicative parameters in lowering drug prices

According to the speaker, «high drug prices were the result of the inefficiency of the «costly» method. As measures to prevent price increases, it is proposed to implement the transition from the «costly» method of registering drug prices to the “indicative” one, as well as introducing the dependency ratio for reproduced drugs and dependence of the price indexation level on the price group of drugs and setting the upper limit, introducing a comparison with prices in other countries for all drugs, regardless of the depth of localization.

3.2. The Federal Antimonopoly Service of Russia recognized as illegal the actions of a legal entity, which entered into circulation of the biologically active additive «AEVIT» with the same name as the medicinal preparation «AEVIT»

The decision of the Federal Antimonopoly Service of Russia on administrative offense of March 15, 2019 in case N 4-14.33-224 /00-08-18

Federal Antimonopoly Service of Russia has established that, given that both the drug and the biologically active additive of the same name are sold in non-prescription pharmacies, the packages of dietary supplements contain information similar to the drug, it is difficult for the consumer who does not have special skills to additive and, moreover, to evaluate the quantitative composition of the drug in relation to the expected therapeutic effect. In this regard, there is a high probability of not only the absence of the expected therapeutic effect but also the possibility of worsening the course of the disease.

Taking into account the fact that unfair competition is not allowed by misleading, including with regard to the quality and consumer properties of the goods offered for sale, the appointment of such goods, the methods and conditions of their manufacture or use, the results expected from the use of such goods, its suitability for certain purposes, Biofarmus LLC was fined 12,000 rubles.

We believe that this decision of the Federal Antimonopoly Service additionally draws attention to the importance of a preliminary assessment of the names and other characteristics of drugs and

dietary supplements in order to mislead the potential consumer regarding his medical and other consumer properties.