



**НИАРМЕДИК**

Россия, 125252, г. Москва,  
ул. Авиаконструктора Микояна, д. 12,  
БЦ «Линкор», корпус «А», 2 этаж

Тел.: +7 (495) 741 49 89  
Факс: +7 (499) 193 43 50

e-mail: info@nearmedic.ru  
www.nearmedic.ru

## MONITORING THE SAFETY OF KAGOCEL®

### 1. Monitoring of the safety of drug circulation

The circulation of all medicines on the market is subject to strict control over their effectiveness and safety of their use.

"Pharmacovigilance or drug safety monitoring is a type of activity aimed at monitoring the effectiveness and safety of medicines and designed to identify, evaluate, and prevent undesirable consequences of the use of medicines" (excerpt from Order No. 1071 of 15.02.2017 "On approval of the procedure for implementing pharmacovigilance").

The ultimate goal of pharmacovigilance is to identify possible cases of inefficiency and adverse reactions to drugs, to assess their frequency, severity, and predisposing factors. Should previously unknown risks of the use of a drug be detected, its Basic Prescribing Information is to be amended: identified possible reactions to the drug and predisposing factors are specified; if necessary, indications for the use of the drug are limited, the list of contraindications may be expanded, changes may be introduced in the dosage, way of administration, etc.

Thus, the task of pharmacovigilance is to protect the rights and interests of patients, providing them with the opportunity to use modern highly effective drugs with the minimal predicted risk of side effects.

Pharmacovigilance is carried out by the Federal Service for Healthcare Supervision of the Russian Federation (Roszdravnadzor) on the basis of information received in the form of:

- messages from subjects of drug application (patients);
- periodic reports on the safety of drugs (hereinafter - PDSR) sent to Roszdravnadzor by holders of registration certificates for medicines (drug manufacturers);
- information received in the course of state control (supervision) in the sphere of circulation of medicines.

Another important tool for monitoring the safety of drug circulation on the market is non-interventional (observational) studies, whereas the manufacturer collects available data obtained as a result of routine clinical practice of using an already registered drug. The key task of observational studies is to control the safety of practical use of the drug. The results of observational studies are subject to regular reporting to Roszdravnadzor.

Thus, monitoring the safety of drug circulation consists of two levels of continuous supervision:

- 1) state supervision: monitoring of patients' messages to Roszdravnadzor and conduct of scheduled audits of the activities of holders of medicines registration certificates;
- 2) monitoring carried out by the holder of the registration certificate, based on patients' requests and the results of implemented observational studies.



**НИАРМЕДИК**

Россия, 125252, г. Москва,  
ул. Авиаконструктора Микояна, д. 12,  
БЦ «Линкор», корпус «А», 2 этаж

Тел.: +7 (495) 741 49 89  
Факс: +7 (499) 193 43 50

e-mail: info@nearmedic.ru  
www.nearmedic.ru

## **2. Monitoring conducted by the holder of the registration certificate**

Monitoring of the safety of medical products is one of the priorities of OOO Nearmedic Plus. Moreover, in accordance with the legislation of the Russian Federation (Federal Law No. 61-FZ "On circulation of medicines"), safety of medicines is the responsibility of their manufacturer, therefore the manufacturer is obliged to constantly monitor the safety of his products.

This is for this reason that OOO Nearmedic Plus has established its Pharmacovigilance Service designed to deal with the safety of the company's medical products, in particular, Kagocel®.

Information about reactions to Kagocel® that requires verification is received by the company spontaneously (from patients using the drug, pharmacists and doctors), as well as collected purposefully (in the course of clinical studies, from industry publications and the Internet). All information received is carefully checked and analyzed.

According to the requirements of the legislation (Roszdravnadzor Order No. 1071 of 15.02.2017 "On approval of the procedure for pharmacovigilance", p.p. 16-18), OOO Nearmedic Plus, like any other pharmacological company, is obliged as follows:

- 1) in case serious adverse events are detected when using a drug, report this for inclusion in the database of Roszdravnadzor automated information system (AIS);
- 2) prepare Periodic Drug Safety Reports (PDSR) on the drug Kagocel®.

The PDSRs that are compiled every three years and sent to Roszdravnadzor, describe in detail and analyze all cases of adverse events, even the least significant ones, registered by the company in the use of the drug.

The latest PDSR was submitted to regulatory authorities by OOO Nearmedic PLUS in September 2018. It contains data on the safety of Kagocel® for the three-year period from 01.07.2015 to 30.06.2018, as well as cumulative data for the entire period of drug circulation on the market.

2.1. Found below are the main cumulative data on the safety of Kagocel®, obtained for the entire period (16 years) of circulation on the market, presented in the PDSR for the period from 01.07.2015 to 30.06.2018. These data once again confirm the high safety profile of the drug.

2.1.1. According to the report, in the 16 years of Kagocel® in the market only 181 adverse reactions have been registered, which accounts for 0.0000905% of the number of packages sold (about 200 million as of October 2019).

2.1.2. Among the identified adverse events, the following were registered: rash of various types, itching, burning sensation on the skin, allergic reaction, rhinorrhea, sneezing, facial



## НИАРМЕДИК

Россия, 125252, г. Москва,  
ул. Авиаконструктора Микояна, д. 12,  
БЦ «Линкор», корпус «А», 2 этаж

Тел.: +7 (495) 741 49 89  
Факс: +7 (499) 193 43 50

e-mail: info@nearmedic.ru  
www.nearmedic.ru

edema, and lacrimation. Most of these, according to the WHO classification, are classified as "rare" (with a rate of 1/10,000 to 1/1000 prescriptions).

2.1.3. The probability of occurrence of those allergic reactions due to possible individual intolerance, is stated in the Basic Prescribing Information of the drug Kagocel®.

2.1.4 Such allergic reactions to the drug remain under the close supervision of the manufacturer and are subject to constant monitoring.

2.1.5. The identified adverse events do not comprise any of those mentioned in mass media by unscrupulous competitors, including those related to reproductive disorders.

2.1.6. Analysis of the information received during the reporting period did not reveal any new risks associated with the use of the drug, and therefore no changes were made to the sections of the Basic Prescribing Information dealing with the safety of the drug.

2.1.7. Neither is there any need to prepare additional explanations or recommendations to improve safety when using Kagocel® 12 mg tablets, since this drug has a well-studied safety profile and is well tolerated when used properly.

2.1.8. The accumulated data on the benefits and safety of Kagocel® based on a 16 year comprehensive analysis of information about the drug indicate a positive benefit-risk ratio.

2.2. The safety of Kagocel® is also confirmed by the results of numerous observational studies conducted by OOO Nearmedic Plus LLC after registration of the drug.

2.2.1. A total of 20 observational studies involving 20,835 patients were conducted within 16 years of receiving the registration certificate. During those studies, only 14 adverse events were identified, the possibility of which was included in the drug's Basic Prescribing Information. In the course of therapy, all adults and children taking the drug showed good tolerance towards Kagocel® in the absence of adverse reactions associated with the drug.

2.2.2. Among the trials, particular mention should go to the large-scale International observational non-intervention study FLU-EE "Treatment of SARS and influenza in routine clinical practice" held at 262 medical centers in Russia, Armenia, Moldova, Georgia (2013-2016) and involving 8,946 patients treated with Kagocel®.

### **3. Monitoring conducted by state supervisory bodies:**

3.1. The Federal Service for Healthcare Supervision of the Russian Federation (Roszdravnadzor) registered only 36 adverse reactions for the entire period of circulation of Kagocel® in the market.

3.2. Registered among the adverse events identified by Roszdravnadzor were mostly allergic reactions due to possible individual intolerance, which is mentioned in the Kagocel® Basic Prescribing Information.



## НИАРМЕДИК

Россия, 125252, г. Москва,  
ул. Авиаконструктора Микояна, д. 12,  
БЦ «Линкор», корпус «А», 2 этаж

Тел.: +7 (495) 741 49 89  
Факс: +7 (499) 193 43 50

e-mail: info@nearmedic.ru  
www.nearmedic.ru

3.3. Among the adverse events identified by Roszdravnadzor, there are none of those mentioned by unfair competitors in media sources, including those related to reproductive disorders.

3.4. It should be noted that the number of adverse events detected by the holder of the registration certificate (181 cases have been registered all in all, including 36 cases from the Roszdravnadzor data base) is significantly higher than the number of adverse events independently detected by Roszdravnadzor (36). This indicates a high level of attention paid by the company to any patient complaints, and their mandatory recording, even if they do not have any direct connection with the action of the drug.

3.5. From April 29 to May 31, 2019, the Federal Service for Healthcare Supervision (Roszdravnadzor) conducted a scheduled field inspection of the Nearmedic Plus company to monitor compliance with mandatory requirements established by the legislation of the Russian Federation in the field of drug circulation (Order 32634 of 08.04.2019).

3.6. The company's audit revealed not a single violation in the procedure for monitoring the safety of medicines: the collection of information on undesirable phenomena and analysis of data related to safety, in order to prevent any negative reactions when using Kagocel®, are carried out in appropriate volumes and in strict accordance with current legislation.

3.7. Currently, Kagocel® 12 mg tablets, produced by Nearmedic Plus, have been duly registered in the Russian Federation, the Republic of Belarus, the Republic of Armenia, Kyrgyz Republic, Kazakhstan, Uzbekistan, Moldova, Georgia, Azerbaijan, and Mongolia.

3.8. In connection with the entry of participants of the Russian pharmaceutical market and the medical community into the new regulatory sphere of the EAEU legislation, OOO Nearmedic Plus also operates under the Rules Of Good Practices of Pharmacovigilance (GVP), approved by the decision of the Council of the Eurasian Economic Commission (EEC) of 03.11. 2016 No.87 (EEU GVP).

3.9. According to the requirements of the EEC Decision, the company regularly collects and analyzes information on adverse reactions to Kagocel® in the CIS and EEU countries.

3.10. In the framework of this monitoring, no reports of adverse reactions from these countries have been received to date.

### **Conclusions:**

1. OOO Nearmedic Plus, as the holder of the registration certificate for Kagocel® medicinal product, carries out its activities in strict compliance with the current legislation of the Russian Federation and the EEU regulating continuous supervision and monitoring of the safety of drug circulation.



## НИАРМЕДИК

Россия, 125252, г. Москва,  
ул. Авиаконструктора Микояна, д. 12,  
БЦ «Линкор», корпус «А», 2 этаж

Тел.: +7 (495) 741 49 89  
Факс: +7 (499) 193 43 50

e-mail: [info@nearmedic.ru](mailto:info@nearmedic.ru)  
[www.nearmedic.ru](http://www.nearmedic.ru)

2. The high level of safety of drug Kagocel® has been confirmed at all levels of supervision and monitoring of the safety of drug circulation (as implemented by state authorities and the own pharmacovigilance service of OOO Nearmedic Plus).
3. All adverse events detected during the period of circulation of drug Kagocel® on the market represent exclusively allergic reactions caused by possible individual intolerance, which is covered in the Basic Prescribing Information of the drug Kagocel®. Most of them, according to the WHO classification, are classified as "rare" (with a rate of 1/10 000 to 1/1000 prescriptions).
4. The total number of adverse events detected during 16 years of Kagocel® circulation on the market is only 181 cases, or 0.0000905% of the number of the drug packages sold during this period (200 million).
5. The identified adverse events comprise none of those mentioned by unscrupulous competitors in mass media, including those related to reproductive disorders.
6. In the 16 years of Kagocel® circulation on the market, the Federal Service for Healthcare Supervision of the Russian Federation has never withdrawn or suspended its registration certificate, did not request the suspension of clinical trials nor did it impose any restrictions on the distribution of the drug.
7. The available summary data obtained over 16 years of Kagocel® circulation on the market by state regulatory authorities and the company's own pharmacovigilance service, convincingly demonstrate the high safety profile of Kagocel®.
8. In the interests of Kagocel® consumers, OOO Nearmedic Plus intends to continue to publish publicly available summary data on the safety of the drug from periodic reports that are regularly provided to the supervisory authorities of the Russian Federation and the EAEU.