



On approval of the Rules for admission to the use, application and monitoring of effectiveness and safety of the use of medicinal products of advanced therapy

Unofficial translation

Order of the Minister of Healthcare of the Republic of Kazakhstan dated December 22, 2020 No. KR HM-312/2020. Registered in the Ministry of Justice of the Republic of Kazakhstan on December 23, 2020 No. 21882

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In accordance with paragraph 2 of Article 243 of the Code of the Republic of Kazakhstan dated July 7, 2020 "On Public Health and Healthcare System" I HEREBY ORDER:

1. To approve the attached Rules for admission to the use, application and monitoring of effectiveness and safety of the use of medicinal products of advanced therapy.

2. The Department of Science and Human Resources of the Ministry of Healthcare of the Republic of Kazakhstan, in the manner established by the legislation of the Republic of Kazakhstan, shall ensure:

1) state registration of this order in the Ministry of Justice of the Republic of Kazakhstan;

2) placement of this order on the Internet resource of the Ministry of Healthcare of the Republic of Kazakhstan after its official publication;

3) submission of information on implementation of the measures provided for in subparagraphs 1) and 2) of this paragraph to the Legal Department of the Ministry of Healthcare of the Republic of Kazakhstan within ten working days after the state registration of this order in the Ministry of Justice of the Republic of Kazakhstan.

3. Control over execution of this order shall be entrusted to the supervising Vice-Minister of Healthcare of the Republic of Kazakhstan.

4. This order shall be enforced upon the expiration of ten calendar days from the date of its first official publication.

*Minister of Healthcare
of the Republic of Kazakhstan*

A. Tsoy

Approved
by the order of the
Minister of Healthcare
of the Republic of Kazakhstan
dated December 22, 2020
No. KR HM-312/2020

Rules for admission to the use, application and monitoring of effectiveness and safety of the use of medicinal products of advanced therapy

Chapter 1. General provisions

1. The Rules for admission to the use, application and monitoring of effectiveness and safety of the use of medicinal products of advanced therapy (hereinafter-the Rules) have been developed in accordance with paragraph 2 of Article 243 of the Code of the Republic of Kazakhstan dated July 7, 2020 "On Public Health and Healthcare System" (hereinafter – the Code) and shall determine the procedure for admission to the use, application and monitoring of effectiveness and safety of the use of medicinal products of advanced therapy.

2. The following terms and definitions are used in these Rules:

1) combination medicinal products of advanced therapy - medicinal products of advanced therapy presented in combination with a medical device;

2) a medicinal product- a product that is or contains a substance or a combination of substances that comes into contact with the human body, intended for the treatment, prevention of human diseases or restoration, correction or change of his/her physiological functions through pharmacological, immunological or metabolic effects, or for diagnosis diseases and human condition;

3) a state expert organization in the field of circulation of medicinal products and medical devices (hereinafter- a state expert organization) - a subject of state monopoly, carrying out production and economic activities in the field of healthcare for ensuring safety, efficiency and quality of medicinal products and medical devices;

4) clinical research - a research with human participation as a subject, conducted to identify or confirm the safety and effectiveness of means, methods and technologies for prevention, diagnosis and treatment of diseases;

5) a medical organization (hereinafter - MO) - an organization of healthcare, the main activity of which is the provision of medical care;

6) medicinal products of advanced therapy (hereinafter- MPAT) – medicinal products obtained by biotechnological or bioengineering way, which offer new opportunities for the treatment of diseases and injuries, including agents for gene therapy, somatic cell therapy, tissue engineering;

7) an informed consent - a procedure for a person's written voluntary confirmation of their consent to receive medical care and (or) participation in a specific research after receiving information about all aspects of medical care and (or) research that are significant for making a decision. An informed written consent shall be drawn up in the form approved by the authorized body.

Chapter 2. Procedure for admission to the use of medicinal products of advanced therapy

3. Medicinal products of advanced therapy, produced in industrial conditions shall be allowed for the use in clinical practice, provided:

1) the presence of positive results of clinical researches;

2) state registration in accordance with the procedure for state registration, re-registration of a medicinal product or medical device, amendments to the registration dossier of a drug or medical device in accordance with paragraph 3 of Article 23 of the Code.

MPAT registered as medicinal products shall be allowed for medical use according to the indications specified in the relevant registration documents.

4. MPAT, produced for individual use, in respect of which positive results of clinical researches have been obtained, shall be admitted to the medical services market on the basis of conclusion of the state expert organization without the state registration procedure.

5. To obtain a conclusion for the use of MPAT produced for individual use, the applicant shall submit to the state expert organization:

1) draft technological regulations for the production of MPAT;

2) a description of physical properties and actions of MPAT;

3) data from scientific and clinical researches on the proposed MPAT and nosologies for the treatment of which it is directed, and (or) systematic reviews summarizing the results of clinical researches at the republican and (or) global levels;

4) information on the qualifications of specialists involved in the production and treatment process;

5) certificate for compliance with the requirements of the Standard of Good Manufacturing Practice (GMP).

6. When issuing a conclusion on the use of drugs produced for individual use, compliance with the requirements that imply an assessment of the risk of MPAT shall be taken into account. To assess the risk of MPAT one should take into account the factors: the source of cells (autologous, allogeneic, xenogenic), the ability to proliferate, differentiate and induce an immune response, the degree of cells change, the combination of cells with bioactive molecules or structural materials, long-term functionality, oncogenicity, method of application. An assessment includes starting material, manufacturing process, product characterization and strategies of control, excipients, scientific researches, and reference materials. To issue a conclusion on the use of a MPAT manufactured for individual use, the following requirements shall be met:

1) MPAT are made for a specific patient according to the individual prescription of an attending physician;

2) MPAT are not manufactured in industrial conditions and are made from biological materials, including cells and tissues. MPAT are subdivided into autologous, allogeneic, or xenogenic origin;

3) MPAT are used in the medical organization in which they were prescribed. The use of MPAT, monitoring of the results shall be carried out personally by the doctor who prescribed the treatment.

When using MPAT in another medical organization related to the patient's place of residence, the administration of MPAT shall be officially confirmed by the attending

physician of this organization, who directly administers the MPAT. The medical organization in which they were prescribed shall provide monitoring of effectiveness and registration of side effects.

7. The period for consideration by the state expert organization of materials of the application for the issuance of a conclusion for the use of MPAT, produced for individual use, and taking the decision to issue or refuse to issue a conclusion shall not exceed thirty calendar days.

8. The state expert organization asks the applicant for additional oral or written explanations, for the provision which no more than thirty working days shall be given, and also involves national experts who do not work in the state expert organization.

9. The state expert organization shall communicate its decision to the applicant within three working days. The applicant who does not agree with the decision of the state expert organization shall require a review. The state expert organization re-examines the initial materials (without submitting additional ones) and makes a final conclusion within thirty calendar days.

10. The use of MPAT produced for individual use shall be approved by the Central or Local commission for bioethics.

Chapter 3. Procedure for the use of medicinal products of advanced therapy

11. When using MPAT containing cells or tissues of human origin, the following conditions shall be ensured:

- 1) donation, collection, storage, and testing of cells and tissues used as raw materials comply with the requirements of the current legislation of the Republic of Kazakhstan;
- 2) there is a registration system that allows tracking in forward and backward directions of cells and (or) tissues used in MPAT, at the stages of donation, production, and administration of the studied product to the patient.

12. When using MPAT requiring special concomitant therapy and (or) the use of surgical procedures that affect the safety and (or) effectiveness of MPAT, the MO provides training and (or) instructing medical personnel on procedures and (or) concomitant therapy before starting the use.

13. The MO on the basis of which the MPAT is produced shall ensure the approval of instructions for the storage, transportation and processing of MPAT, including a description of risks for the personnel working with MPAT, as well as the risks to the environment.

14. For MPAT requiring controlled temperature conditions during transportation and (or) storage prior to its use, the medical organization on the basis of which MPAT is produced and (or) used shall ensure the availability of registration and (or) monitoring of temperature and fulfillment of the required temperature conditions.

15. For MPAT with a limited shelf life, the instructions for the use of drugs indicate the time frame from production to the use of drugs.

Chapter 4. Procedure for monitoring the effectiveness and safety of the use of medicinal products of advanced therapy

16. In the organization carrying out the production of MPAT (hereinafter -the production organization) and the MO, where the administration and use of MPAT is carried out, a documentation system is being introduced that ensures the traceability of manufacture, application and results of the use of MPAT. The documentation system covers the entire production process and includes the characteristics of the finished MPAT, labeling and description of packaging materials, intermediate products, instructions and procedures for manufacturing operations, protocol, doctor's prescription.

17. The MPAT label (or the attached instructions for the use of MPAT) includes the following information:

- 1) the name of the drug;
- 2) the name of the MO in which the drug was prescribed;
- 3) identification code of the drug and (or) packaging;
- 4) the name and registration number of the patient to whom the drug was prescribed;
- 5) the name and registration number of the doctor;
- 6) the name and quantity of active substances;
- 7) type of cells and (or) tissues;
- 8) dosage form;
- 9) a list of excipients, including canning systems;
- 10) the shelf life of the drug;
- 11) special storage conditions;
- 12) the results of examination for transfusion infections.

18. The cells that are in the composition of the MPAT shall be taken from volunteers and a donor.

19. Transportation of MPAT shall be carried out in accordance with the requirements for storage conditions according to the instructions for medical use developed by the manufacturers.

20. The MO using MPAT appoints a pharmacovigilance officer for MPAT, who ensures:

- 1) analysis and comparison of all received information on suspicious adverse reactions;
- 2) a report on the effectiveness and safety of MPAT for the production organization during the first two years after the introduction of MPAT.

21. The MO shall inform the manufacturing organization of all serious adverse reactions in the course of treatment with the use of MPAT.

22. The informed consent of the patient (his/her legal representative) to the use of MPAT indicates the essence of the proposed treatment, the general characteristics of the MPAT, the expected results and possible risks in the treatment, as well as the potential advantages of MPAT over standard treatment methods.

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