



CABINET OF MINISTERS OF UKRAINE

DECREE

of December 29, 2021 № 1446

Kyiv

Some issues of state registration of medicinal products, vaccines or other medical immunobiological products for treatment and/or specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2 subject to obligations for emergency medical use

{amended by the Decree of the Cabinet of Ministers
№ 471 dated 15.04.2022}

According to Article 9² of the Law of Ukraine “On Medicines”, the Cabinet of Ministers of Ukraine **decides:**

1. To approve the Procedure for the state registration of medicinal products, vaccines or other medical immunobiological products for treatment and/or specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2 subject to obligations for emergency medical use (attached).

2. To specify that:

Issues of the responsibility of manufacturers of medicinal products, vaccines or other medical immunobiological products for treatment and/or specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2, supplied through the COVAX mechanism, and requirements to texts of instructions for use and labelling of the immediate and outer (if any) packaging of such medicinal products, vaccines or other medical immunobiological products are regulated by agreements signed by Ukraine through the COVAX mechanism. The State Expert Center of the Ministry of Health of Ukraine shall conduct an expert evaluation of the benefit/risk balance and verification of the authenticity of registration materials during the state registration of such medicinal products, vaccines or other medical immunobiological products, which are to be supplied through the COVAX mechanism in Ukraine, and expert evaluation in case of extension of the validity period of registration certificate and in case of introduction of changes to registration materials free of charge;

registration of medicinal products, vaccines or other medical immunobiological products for treatment and/or specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2, subject to obligations for emergency medical use, the development and/or production of which has been carried out in a state recognized by Ukraine as an aggressor state, is prohibited.

2¹. During the period of martial law and/or within six months from the date of termination or abolition of martial law to extend the period of use, import and circulation in Ukraine of medicinal products, vaccines or other medical immunobiological products for treatment and/or specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2, subject to obligations for emergency medical use for which the registration certificate has expired during the

martial law and/or within six months from the date of termination or abolition of the martial law, by extending the validity period of registration certificate for such medicinal product, vaccine or other medical immunobiological product for one year from the date of expiration of the registration certificate and/or for the period of martial law, and/or within six months from the date of termination or abolition of martial law, with entering information on extension the validity period of the registration certificate for such a medicinal product, vaccine or other medical immunobiological product for the treatment and/or specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2, subject to obligations for emergency medical use, to the State Register of Medicinal Products of Ukraine.

Updated information in the State Register of Medicinal Products of Ukraine on the extended validity period of the registration certificate for medicinal product, vaccine or other medical immunobiological product specified in the first paragraph of item 2-1 of this Decree, certifies the validity of state registration of such medicinal product, vaccine or other medical immunobiological product and does not require the issuance of a new or replacement of a valid registration certificate.

Since the date of termination or abolition of martial law, but not later than six months from the date of termination or abolition of martial law the holders of registration certificates shall submit to the State Expert Center of the Ministry of Health of Ukraine a letter on extension the validity period of the registration certificate for registered medicinal product, vaccine or other medical immunobiological product for the treatment and/or specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2, subject to obligation for emergency medical use.

{Item 2¹ is added to the Decree in accordance with the Decree of the Cabinet of Ministers № 471 of 15.04.2022 - valid for six months from the date of termination or abolition of martial law}

3. The Decree of the Cabinet of Ministers of Ukraine of February 8, 2021 № 95 “Some issues of state registration of vaccines or other medical immunobiological products for specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2 subject to obligations for emergency medical use” is revoked (Official Gazette of Ukraine, 2021, № 15, p. 584).

D. Shmygal
Prime Minister of Ukraine

APPROVED

by the Decree of the Cabinet of
Ministers of Ukraine
of December 29, 2021 № 1446

PROCEDURE

for the state registration of medicinal products, vaccines or other medical immunobiological products for treatment and/or specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2 subject to obligations for emergency medical use

General

1. This Procedure establishes the mechanism of the state registration of medicinal products, vaccines or other medical immunobiological products for treatment and/or specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2, subject to obligations for emergency medical use (hereinafter - the state registration of medicinal products and medical immunobiological products for emergency use).

2. The state registration of medicinal products and medical immunobiological products for emergency use is conducted by the Ministry of Health of Ukraine (MoH) based on the application and substantiated opinion of the State Expert Center of the Ministry of Health of Ukraine (hereinafter - the Center) considering the results of benefit/risk expert assessment and verification of registration materials of medicinal products and medical immunobiological products for their authenticity, taking into account certain obligations (except for vaccines or other immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine).

MoH conducts the state registration of medicinal products and medical immunobiological products for emergency use if there is a lack of comprehensive clinical data on the safety and efficacy, provided the following requirements are met:

the known and potential benefits of medicinal products and medical immunobiological products when used to treat and/or prevent acute respiratory disease COVID-19 caused by the coronavirus SARS-CoV-2 outweigh the known and potential risks of using such medicinal products or other medical immunobiological products;

the applicant - a legal or natural person responsible for the quality, safety and efficacy of medicinal products and medical immunobiological products and conducting pharmacovigilance (hereinafter - the applicant) is obliged to provide the Center with the comprehensive data after completion of the appropriate clinical trials during the validity period of registration certificate for such medicinal product and medical immunobiological product.

Peculiarities of state registration of medicinal products, vaccines or other medical immunobiological products for treatment and/or specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2 subject to obligations for emergency medical use

3. The application for state registration of medicinal products and medical immunobiological products subject to the obligations for emergency medical use (hereinafter - the application for state registration for emergency use), drawn up in the form given in Annex 1, submitted by the applicant to the MoH, shall specify the obligations of the applicant as follows:

to conduct post-registration safety studies in availability of risks of medicinal products and medical immunobiological products registered for emergency use;

to conduct post-registration efficacy studies when the understanding of disease or clinical methodology indicates the need for a substantial revision of previous efficacy evaluations.

4. The application for state registration for emergency use submitted to the Center shall be supplemented by the following:

1) for medical immunobiological products used for specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2 - a document confirming the decision to grant an emergency use authorization or conditional marketing authorization in the appropriate country or conditional marketing authorization by the competent authority of the European Union (or other essentially identical decision under the applicable law of the United States of America, the United Kingdom, the Swiss Confederation, Japan, Australia, Canada, the People's Republic of China, Israel or via a centralized procedure by the competent authority of the European Union in accordance with the national legislation of the country of authorization or the European Union) or decision of the World Health Organization pertinent to prequalification of medical immunological products for emergency use on the date of application for state registration for emergency medical use, certified by the signature of the applicant or his authorized representative;

for medicinal products used for treatment of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2 - a document confirming the decision to grant an emergency use authorization or conditional marketing authorization in the appropriate country or conditional

marketing authorization by the competent authority of the European Union (or other essentially identical decision under the applicable law of the United States of America, the United Kingdom, the Swiss Confederation, Japan, Australia, Canada, Israel or via a centralized procedure by the competent authority of the European Union in accordance with the national legislation of the country of authorization or the European Union) or decision of the World Health Organization pertinent to prequalification of medical products for emergency use on the date of application for state registration for emergency medical use, certified by the signature of the applicant or his authorized representative;

2) an assessment report for medicinal products and medical immunobiological products drawn up by the regulatory authority of the country where the medicinal products and medical immunobiological products are registered (if such a document is provided for by the legislation of the appropriate country; if there is no such document the appropriate mark shall be inserted in the application for the state registration for emergency medical use);

3) a risk assessment and management document approved by a decision on granting an emergency use authorization or conditional marketing authorization in the appropriate country or conditional marketing authorization by the competent authority of the European Union (if such a document is provided for by the legislation of the appropriate country; if there is no such document the appropriate mark shall be inserted in the application for the state registration for emergency use);

4) instructions for use of the medicinal products and medical immunobiological products, set out in the original language (a language other than the state one) (if available, if such a document is provided for by the legislation of the appropriate country; if there is no such document the appropriate mark shall be inserted in the application for the state registration for emergency use);

5) summary of product characteristics for medicinal products and medical immunobiological products in the original language (a language other than the state one) (if available, if such a document is provided for by the legislation of the appropriate country; if there is no such document the appropriate mark shall be inserted in the application for state registration for emergency use);

6) layout of the packaging mockup(s) of the medicinal product and the text(s) of the labeling of the immediate and outer (if any) packaging of the medicinal products and medical immunobiological products. For the purposes of state registration for emergency use the applicant has the right to submit several such mockups and labeling texts at the same time to ensure the delivery as prompt as possible in packaging and with the labeling available at the time of delivery;

7) translations of the text(s) of the labeling of the immediate and outer (if any) packaging, instructions for use, summary of product characteristics for medicinal products and medical immunobiological products in the state language, which are certified by signature of the applicant or his authorized representative;

8) for medical immunobiological products - a written commitment of the manufacturer to produce medical immunobiological products concerned to supply them in Ukraine at the same production capacities as those employed for production of these medical immunobiological products intended for the use in the appropriate country of authorization (the United States of America, the United Kingdom, the Swiss Confederation, Japan, Australia, Canada, the People's Republic of China, Israel or European countries);

for medicinal products - a written commitment of the manufacturer to produce medicinal product concerned to supply it in Ukraine at the same production capacities as those employed for production of this medicinal product intended for the use in the appropriate country of authorization (the United States of America, the United Kingdom, the Swiss Confederation, Japan, Australia, Canada, Israel or European countries);

9) a certified copy of document confirming the compliance of manufacturing conditions for the medicinal products and medical immunobiological products submitted for state registration for emergency use with the requirements to manufacture of medicinal products and medical immunobiological products in Ukraine issued by the State Service of Ukraine for Medicinal

Products and Narcotics Control (hereinafter – Derzhliksluzhba) or Derzhliksluzhba's decision on recognition of the results of GMP compliance inspections conducted by the national competent authority of the country of manufacture, which is issued according to the procedure established by the MoH.

10) the materials of registration dossier submitted for emergency use authorization or conditional marketing authorization in appropriate country of authorization.

With the purpose to enable a proper expert assessment of the benefit/risk balance of medicinal products and medical immunobiological products during the state registration for emergency use, the applicant may provide other registration materials that were the basis for the emergency use authorization of these medicinal products and medical immunobiological products issued by the appropriate competent regulatory authority. Such materials may include links to the websites of these regulatory authorities and/or websites of organizations that summarize data on preclinical and clinical trials of medicinal products and medical immunobiological products.

If the applicant or his authorized representative submits all the materials specified in subitems 1-10 of this item, any other materials/letters from the applicant or his authorized representative and/or written commitments shall not be required by the Center.

Annexes to the application for state registration for emergency use may be submitted to the Center in paper or electronic format at the applicant's discretion.

Registration materials are submitted to the Center in Ukrainian or English at the applicant's discretion. If the materials are submitted in any other language, at the Center's request, the applicant or the applicant's representative shall provide their translation into Ukrainian or English.

5. Upon receipt of the application for state registration of medicinal products and medical immunobiological products for emergency use, the MoH shall send a copy of the application for state registration of medicinal products and medical immunobiological products concerned for emergency use followed by a MoH's letter of referral to the Center within one working day.

6. The Center shall conduct expert assessment of the benefit/risk balance of the medicinal products and medical immunobiological products and verifies the authenticity of registration materials for the purpose of state registration of medicinal products and medical immunobiological products for emergency use within five working days from the date of receipt of the MoH's letter of referral and receipt from the applicant of the materials specified in item 4 of this Procedure. Based on the results of the expert assessment of the benefit/risk balance and verification of authenticity of registration materials, the Center shall draw up a substantiated opinion according to the form given in Annex 2 (hereinafter - the opinion on registration of medicinal products and medical immunobiological products for emergency use) and send it to the MoH together with the verified authentic translations of the text(s) of the labeling of the immediate and outer (if any) packaging, instructions for use, summary of product characteristics (if any) for the medicinal products and medical immunobiological products in the state language.

In case of a negative opinion on the registration of medicinal products and medical immunobiological products for emergency use, the Center submits a motivated justification for its proposal.

7. Based on the application and opinion on registration of medicinal products and medical immunobiological products for emergency use prepared by the Center the MoH shall make a decision on state registration of medicinal products and medical immunobiological products for emergency use or refusal of such registration within three working days.

If the Center's opinion contains information on discrepancies between the registration dossier materials and the application submitted by the applicant or his authorized representative and/or other materials attached to the application for state registration for emergency use, the applicant or his authorized representative may submit to the MoH an explanation of such discrepancies in order

to take them into account when the MoH decides on the state registration of medicinal products and medical immunobiological products for emergency use.

The instruction for medical use is approved by the decision on state registration of medicinal products and medical immunobiological products for emergency use and a registration number is assigned to the medicinal products and medical immunobiological products, which is entered into the State Register of Medicinal Products of Ukraine together with information about the medicinal product according to the list of information specified by legislation. In the State Register of Medicinal Products of Ukraine, the medicinal products and medical immunobiological products are registered in accordance with the requirements of this Procedure and are specified as a “medicinal product for emergency use”.

8. The fact of state registration of medicinal products and medical immunobiological products for emergency use is confirmed by a registration certificate in the form given in Annex 3. The registration certificate is issued for a period of one year. The validity period of the registration certificate may be extended annually for the next year provided that the Center does not have information on the revealed negative benefit/risk balance as well as pharmacovigilance data indicating the identified harmful properties. The total validity period of the registration certificate may not exceed the validity period of the emergency use authorization granted by the appropriate competent authority.

In order to extend the validity period of registration certificate, the applicant or his authorized representative shall submit a letter to the Center in any form not later than one month before the expiration of the registration certificate.

The registration certificate may contain obligations imposed on the holder of the registration certificate for medicinal products and medical immunobiological products as follows:

to conduct the post-registration safety studies in availability of risks of medicinal products and medical immunobiological products registered for emergency medical use;

to conduct post-registration efficacy studies when understanding of the disease or clinical methodology indicates the need for a substantial revision of previous efficacy evaluations.

9. The state registration of medicinal products and medical immunobiological products for emergency use may be refused only in the case of: failure to submit the appropriate materials provided for in item 4 of this Procedure, or incomplete materials, or discrepancies revealed in the submitted materials affecting efficacy, safety and quality of the medicinal products and medical immunobiological products, or inauthenticity of translation of the text (texts) of the package (packages) labeling, the instructions for use or a summary of product characteristics (if any).

When the applicant of the medicinal products and medical immunobiological products registered according to this Procedure does not fulfill the obligations specified in item 2 of this Procedure the state registration of the medicinal products and immunobiological medicinal products concerned shall be terminated by the MoH prior to expiration of the validity period of registration certificate.

10. Changes in registration materials shall be introduced according to the Procedure for Conducting Expert Evaluation of Registration Materials Pertinent to Medicinal Products, which are Submitted for State Registration (Re-Registration) and Expert Evaluation of Materials about Introduction of Changes to the Registration Materials during the Validity Period of Registration Certificate approved by the MoH (hereinafter - the Expert Evaluation Procedure), based on the decision made by the same competent authority, which was submitted during the state registration procedure for emergency use.

11. During the validity period of the registration certificate, the applicant shall:

inform the Center about adverse reactions to the medicinal products according to the procedure and within the timeframe established by the Pharmacovigilance Procedure, approved by the MoH;

provide the Center with information about the clinical trials completed, including their results, which are to be the basis for expert assessment of the benefit/risk balance.

Peculiarities of state registration of vaccines or other medical immunobiological products for specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2 subject to obligations for emergency medical use having a full production cycle or manufactured from "in bulk" products in Ukraine

12. The state registration of vaccine or other medical immunobiological product for specific prevention of acute respiratory disease COVID-19 caused by coronavirus SARS-CoV-2 subject to obligations for emergency medical use having a full production cycle or manufactured from "in bulk" products in Ukraine (hereinafter - medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine) is conducted by the MoH based on the application and substantiated opinion of the Center considering the results of benefit/risk expert assessment and expert evaluation of registration materials and results of quality control of medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine taking into account certain obligations. MoH conducts the state registration of medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine if there is a lack of comprehensive clinical data on the safety and efficacy of medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine, provided the following requirements are met:

data are available on the successful preclinical trials/studies, certain phases of clinical trials/studies and the results obtained cumulatively contain scientifically based evidence, including data from adequate and well-controlled studies, that suggest that medicinal products, vaccines or other medical immunobiological products may be effective for emergency medical use during an emergency situation and/or quarantine;

the known and potential benefits of medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine when used outweigh the known and potential risks of using such medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine;

the applicant is obliged to provide the Center with the comprehensive data obtained from the appropriate clinical trials of medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine during the period specified by the MoH, which should be the basis for expert assessment of the benefit/risk balance.

13. The application for state registration of medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine, drawn up in the form given in Annex 4, submitted by the applicant to the MoH, shall specify the obligations of the applicant as follows:

to conduct post-registration safety studies in availability of risks of medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine registered for emergency use;

to conduct post-registration efficacy studies when the understanding of disease or clinical methodology indicates the need for a substantial revision of previous efficacy evaluations.

14. At the applicant's request, the state registration of the active pharmaceutical ingredient and/or "in bulk" products which are used to produce the finished medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine submitted for registration may be carried out simultaneously with the registration of the finished medical immunobiological product having a full production cycle or manufactured from "in bulk" products in Ukraine.

15. Upon receipt of the application for state registration of medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine, the MoH shall send a copy of such application followed by a MoH's letter of referral to the Center within one working day.

16. The Center shall conduct expert evaluation of registration materials pertinent to medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine according to the Expert Evaluation Procedure with regard to the circumstances specified in item 12 of this Procedure.

The scope and basic requirements for the registration dossier materials attached to the application for state registration submitted by the applicant or his authorized representative to the Center shall be determined by the Expert Evaluation Procedure with regard to the circumstances specified in item 12 of this Procedure.

The Center shall conduct expert assessment of the benefit/risk balance of the medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine and expert evaluation of registration materials within five working days from the date of receipt of the MoH's letter of referral and receipt from the applicant of the materials of registration dossier.

Based on the results of the expert assessment of the benefit/risk balance and expert evaluation of registration materials, the Center shall draw up a substantiated opinion according to the form given in Annex 5 (hereinafter - the opinion on medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine for emergency use) and send it to the MoH.

17. Based on the application and opinion on medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine for emergency use prepared by the Center the MoH shall make a decision on state registration of medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine for emergency use or refusal of such registration within three working days. The instruction for medical use is approved by the decision on state registration of medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine for emergency use and a registration number is assigned to the medicinal product, which is entered into the State Register of Medicinal Products of Ukraine together with information about the medicinal product according to the list of information specified by legislation. In the State Register of Medicinal Products of Ukraine, the medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine are registered in accordance with the requirements of this Procedure and are specified as a "medicinal product for emergency use".

18. The fact of state registration of medical immunobiological products having a full production cycle or manufactured from "in bulk" products in Ukraine for emergency use is confirmed by a registration certificate in the form given in Annex 3. The registration certificate is issued for a period of one year. The validity period of the registration certificate may be extended annually for the next year provided that the Center does not have information on the revealed negative benefit/risk balance as well as pharmacovigilance data indicating the identified harmful properties.

The registration certificate may contain obligations imposed on the holder of the registration certificate of medical immunobiological product having a full production cycle or manufactured from "in bulk" products in Ukraine as follows:

to conduct the post-registration safety studies in availability of risks of medical immunobiological product having a full production cycle or manufactured from "in bulk" products in Ukraine registered for emergency medical use;

to conduct post-registration efficacy studies when understanding of the disease or clinical methodology indicates the need for a substantial revision of previous efficacy evaluations.

19. The state registration of medical immunobiological product having a full production cycle or manufactured from "in bulk" products in Ukraine for emergency use may be refused only in the case of: failure to submit the appropriate materials provided by the Expert Evaluation Procedure with regard to the circumstances specified in item 12 of this Procedure or incomplete materials.

When the applicant of the medical immunobiological product having a full production cycle or manufactured from "in bulk" products in Ukraine registered according to this Procedure does not fulfill the obligations specified in item 12 of this Procedure the state registration of such medical immunobiological product shall be terminated by the MoH prior to expiration of the validity period of registration certificate.

20. Changes in registration materials shall be introduced according to the Expert Evaluation Procedure.

21. During the validity period of the registration certificate, the applicant shall:

perform pharmacovigilance of the medical immunobiological product having a full production cycle or manufactured from "in bulk" products in Ukraine according to the Pharmacovigilance Procedure, approved by the MoH;

provide the Center with information about the clinical trials completed, including their results, which are to be the basis for expert assessment of the benefit/risk balance.