CInMED
Institute for Medicines and Medical Devices of Montenegro

INSTRUCTIONS FOR SUBMITTING THE APPLICATION AND DOCUMENTATION FOR THE RENEWAL OF MARKETING AUTHORISATION FOR MEDICINES FOR HUMAN USE

In accordance with Articles 77 and 78 of the Law on Medicines ("*Official Gazette of Montenegro*" No. 14/26) (hereinafter: Law on medicines) the marketing authorization holder (hereinafter: MAH) shall submit to the Institute for Medicines and Medical Devices (hereinafter: CInMED) an application for renewal of the marketing authorisation no later than nine months before the expiry of a MA granted for five years, or no later than six months before the expiry of a conditional MA.

The application shall be submitted to the registry office of the CInMED or via the CInMED portal for electronic submission of documentation.

Documentation shall be submitted exclusively in electronic format, in the following file formats: *Word* documents (docx), *Excel* worksheets (xlsx) and PDF, following the CTD format. Document names must be specified so as to clearly and unambiguously describe the content of the document.

If the documentation is submitted via the CInMED registry office, in addition to the documentation submitted in electronic form, the following shall also be provided:
- a cover letter in paper form (signed and stamped by the applicant), in two copies;
- a completed Application Form for the renewal of marketing authorisation, in paper form (signed and stamped by the applicant) or in electronic form signed with an electronic signature and electronic seal, in accordance with the law governing electronic identification and electronic documents.

In accordance with Article 34 of the Law on medicines, the CInMED, in the procedure of granting a marketing authorisation, does not assess whether there is an infringement of intellectual or industrial property rights. Therefore, in the documentation submitted with the application for renewal of the marketing authorisation, no designations indicating protection of the medicinal product name shall be stated.

The following documentation shall be submitted with the application for renewal of the MA:

MODULE 1 – Administrative data

1.0. Cover letter of the application for the renewal of marketing authorisation on the form available on CInMED portal.

1.1. Content

1.2. Completed Application form for the renewal of the marketing authorisation**,** prepared using the template available on the CInMED portal.
- The form itself must not be altered. Sections of the form that are not applicable to the application shall be marked as N/A (Not Applicable) – parts that cannot be filled in due to lack of data must not be deleted;
- The form shall be filled in electronically, signed by the person responsible for the renewal of the marketing authorisation, with the seal of the applicant or signed with an electronic signature and

electronic seal in accordance with the law governing electronic identification and electronic documents (the form shall not be submitted as a scanned copy of an electronically signed document);
- MAH shall submit a completed application form for each pharmaceutical form, strength, type and pack size of the medicinal product;
- When entering data on the pharmaceutical form, packaging and route of administration, it is necessary to use standard EDQM terms;
- In the section "*List of variations*" of the form, a chronological list shall be provided of all variations submitted/approved by CInMED (type IA/IB, type II, variations for which a new authorization has been issued), indicating the reference number under which each variation was received in CInMED. The list must also include information on all notifications, urgent safety measures and PSURs submitted during the period of validity of the marketing authorization (unless they are part of any of the variations listed). The information may also be provided as an annex to the application form, in a separate document entitled *List of variations in Montenegro.*

As an attachment to the application form, the following documentation shall also be submitted in electronic format:

- **Overview of the marketing authorisation status of the medicinal product in other countries**
  An overview shall be provided of the countries in which a marketing authorisation has been graned, as well as information on the countries where the medicinal product has been placed on the market, including the date of first placing on the market. If the application for MA has been refused in any country, or a marketing authorisation has been revoked by a competent authority, a justification for such refusal or revocation of the marketing authorisation shall be provided.

- **Chronological list of all conditions/obligations after the issuance/last renewal of marketing authorisation,** with the date of submission of documentation to CInMED (if applicable).

- **Revised list of remaining conditions and specific obligations** (if applicable)

- **Chronological list of all variations** submitted/approved in the EU (if applicable)

- **Documentation for the manufacturing site(s) of the active substance and a medicinal product**
  Flow chart for Montenegro – The chart must indicate the name and addresses of the manufacturers involved in all stages of active substance manufacturing (including the sites for the manufacture of active substance intermediates, as well as micronisation and sterilisation sites, where applicable) and of the finished product. In cases where the flow chart lists only batch release sites for the EU, it is necessary to explicitly indicate whether the same manufacturers are responsible for batch release in Montenegro as well.

  For all sites involved in the manufacturing process of the active substance and intermediates (including the site of micronization, where applicable), a Qualified Person (QP) declaration confirming

compliance with GMP requirements shall be provided, from:

- the manufacturer which uses the active substance as a starting material (if established in the EEA member states), and
- the manufacturer of a medicinal product responsible for batch release.

It is also possible to submit a single QP declaration on behalf of manufacturers of a medicinal product who are required to provide a QP declaration. The QP declaration shall be prepared in accordance with the current version of EMA guideline: *Guidance for the template for the qualified person's declaration concerning good manufacturing practice (GMP) compliance of active substance manufacture "The QP declaration template*".

For manufacturing sites of sterile active substances, a valid GMP certificate issued by the regulatory authority of an EEA Member State or an EUMRA country, shall also be provided.

For all sites involved in the manufacturing process of the medicinal product, it is necessary to submit a valid evidence of compliance with Good Manufacturing Practice requirements (GMP certificate) issued by the competent authority of an EEA Member state, EUMRA or CInMED.

- **Information and documentation about the MAH and the person responsible for renewal of the marketing authorisation and pharmacovigilance** (it is necessary to submit the documentation, in case that the MAH has not submit it along with some of previous applications for MA, amendments to it, or its renewal). The documentation shall be submitted in accordance with the guidance *Manner of submitting application and documentation for obtaining marketing authorisation for medicines for human use,* available on the CInMED portal.

- A statement undertaking to provide the standards and samples necessary for quality control, upon the request of the CInMED, no later than within 30 days.

1.3. Summary of product characteristics, labelling and Package leaflet

A statement from the MAH shall be provided confirming that the product information has been updated in accordance with the latest scientific knowledge, including the conclusions of assessments and recommendations published in the European Union. The statement shall include information on when the product information was last updated, with reference to the latest variation through which the change was implemented.

During the renewal procedure, CInMED may, based on the assessment of the submitted documentation, request amendments to the texts of the SmPC, labelling and package leaflet. In such cases, the MAH shall be required to submit a separate application for the approval of a variation, in accordance with the guidance *Manner of submitting application and documentation for variations*, available on the CInMED portal.

1.4. Information on experts

Curricula Vitae (CVs) of the experts who prepared the expert summaries on the pharmaceutical-chemical-biological, pharmacological-toxicological, and clinical documentation shall be submitted, together with signed declarations of the experts indicating the date of preparation of the submitted expert summaries.

1.8. Pharmacovigilance documentation

- Summary of the EU/global and the local PSMF. The summary PSMF shall contain the information prescribed by the Law on Medicines, Article 34, paragraph 1, point 12;
- The most recent PSUR/PBRER for medicinal products for which submission is required under the Law on Medicines. The submission frequency of the PSUR/PBRER shall be aligned with the EURD list. If the submission frequency of the PSUR/PBRER is not determined by the EURD list, the marketing authorization holder is obliged to submit to CInMED, together with the PSUR/PBRER, a statement on the proposed submission frequency of the PSUR/PBRER.
- The most recent RMP. For medicinal products without an RMP, the marketing authorization holder shall provide a statement declaring that the RMP has not been submitted and explaining the reasons for its non-submission (e.g. not required, in preparation, etc.).
- A statement on additional risk minimization measures, including a plan for their implementation, if such implementation is required.

MODULE 2

For medicinal products for which a marketing authorisation has been granted via the centralised procedure (CP) in the EU, Module 2 as submitted to and approved by the European Medicines Agency (EMA) in the context of the latest renewal od the MA shall be provided, as follows:

2.3. Addendum to Quality Overall Summary *(Addendum to QOS)*

2.4. Addendum to Non-clinical Overview *(Addendum to NCO)*

2.5. Addendum to Clinical Overview *(Addendum to CO)*

In addition, a list of all approved variations under the CP shall be provided, together with their regulatory status in Montenegro.

For medicinal products authorised via the decentralised procedure (DCP) or mutual recognition procedure (MRP) in the European Union, which have been granted a marketing authorisation in Montenegro under the accelerated assessment procedure pursuant to Article 54 of the Law on medicines, as well as for medicinal products authorised under abridged applications, Module 2 shall not be required. Instead, the following documentation shall be submitted:

- **Quality Expert Statement**, confirming that the quality of the medicinal product is regularly updated through variation procedures in order to take into account scientific and technical progress, and that the quality of the medicinal product is in compliane with applicable EU quality guidelines;

- **Clinical Expert Statement**, confirming that:
  - all relevant data necessary for the assessment of the risk - benefit balance of the medicinal product have been submitted to CInMED;
  - no new non-clinical or clinical data are available that would alter or lead to a new assessment of the risk - benefit balance of the medicinal product;
  - information on proposed or implemented measures for the safe use of the medicinal product have been submitted, and that the marketing authorisation, from a safety perspective, may be renewed for a further five years or for an unlimited period, as applicable;
  - the product information is in line with current scientific knowledge, including relevant conclusions and recommendations applicable in the European Union.

- **Final Renewal Assessment Report** issued in the DCP or MRP procedure, where applicable; and

- **Statement from the MAH** confirming that, upon request of CInMED, the complete Module 2 documentation will be submitted.

If, during the assessment of the documentation, it is considered that the submitted statements are not sufficient, CInMED shall require the submission of the full Module 2 documentation.

Where, following a previous renewal procedure, an additional renewal of the marketing authorisation has been required for pharmacovigilance-related reasons, the complete Module 2 shall be submitted, irrespective of the exemptions set out above.

In all other cases, i.e. for medicinal products not falling within the above-mentioned categories, the following documentation shall be submitted:
2.3. Addendum to Quality Overall Summary *(Addendum to QOS)*
2.4. Addendum to Non-clinical Overview *(Addendum to NCO),* if applicable
2.5. Addendum to Clinical Overview *(Addendum to CO).*