Pursuant to Article 24 and paragraph 7 of the Law on Medicines („Official Gazette of Montenegro“ No 56/11 and 6/13), the Ministry of Health hereby issues the

RULEBOOK
ON MORE DETAILED CONDITIONS AND MANNER OF ENTERING A MEDICINE INTO THE REGISTER OF HOMEOPATHIC MEDICINES

(„Official Gazette of Montenegro” No 06/15 from 10 February 2015)

I GENERAL PROVISIONS

Article 1

Homeopathic medicines shall be entered into the Register of homeopathic medicines (hereinafter: Register) under conditions defined by this Rulebook.

Article 2

The terms from this Rulebook used for natural persons in masculine gender shall include the same terms in feminine gender.

II ENTERING INTO THE REGISTER AND REMOVING FROM THE REGISTER

Article 3

In order to enter a homeopathic medicine into the Register, an application on an application form containing data listed below shall be submitted:

1) name of a medicine;
2) name of homeopathic raw material(s);
3) a pharmaceutical form, route of administration, data on the packaging, degree of dilution;
4) data on the composition of homeopathic medicine;
5) data on the manufacturer (name, address and manufacturing site);
6) proposed mode of dispensing;
7) date and signature of the person responsible for application for entering into the Register.

The application referred to in paragraph 1 of this Article may refer to a single pharmaceutical form in different degrees of dilution and packaging which are prepared from the same homeopathic ingredients (homeopathic stock).

The application referred to in paragraph 1 of this Article shall be accompanied by the evidence on paid fees.

The application form for entering into the Register is available on the portal of the Agency for Medicines and Medical Devices (hereinafter: the Agency)

Article 4

The application referred to in Article 3 of this Rulebook shall be accompanied by the documentation on a homeopathic medicine, which includes:

1) scientific name or name given in a pharmacopoeia of the homeopathic stock or stocks, with a description of all proposed routes of administration, pharmaceutical forms and degree of dilution;

2) data that describe how homeopathic stock or stocks have been obtained and their quality controlled and bibliographic data justifying its/their homeopathic use;
3) data to describe the measures taken to ensure the absence of disease agents;
4) data on the manufacture and control of quality for each pharmaceutical form and description of the method of dilution and potentization;
5) manufacturing authorization issued by the competent authority in the country of manufacturer and a certificate on Good Manufacturing Practice of the competent authority or a certificate on good manufacturing practice of regulatory authorities of the European Union Member States;
6) list of countries which authorized a medicine for placing on the market, or entered it in the Register, or where it is in the process of obtaining appropriate authorization, as well as a list of countries in which the medicine is marketed, as well as data on rejecting the application in a certain country and reasons for such decision;
7) proposed inner and outer packaging and the patient information leaflet, if applicable;
8) data on stability of a medicine

Article 5

Documentation on the homeopathic medicine referred to in Article 4 of this Rulebook shall be submitted in the form of the Common Technical Document (CTD dossier), with specific requirements for homeopathic medicines, in accordance with the regulation that determines conditions for issuance of marketing authorization for a medicine.

The specific requirements of paragraph 1 of this Article shall apply to:
1) pharmaceutical-chemical-biological and microbiological documentation;
2) pharmacological and toxicological documentation.

Requirements for the pharmaceutical-chemical and biological and microbiological documentation, refer to:

- terminology: Latin name of the homeopathic stock must be in accordance with the Latin title of the European Pharmacopoeia, or in an official pharmacopoeia of the Member State of the European Union. If applicable, traditional name used in the European Union should be stated;
- data on the control of starting materials: documentation on starting substances, i.e. all used materials, including raw materials and intermediates, in the preparation of the final dilution that enters into the composition of a finished product, together with data on the homeopathic stock. It is necessary to determine the content of toxic ingredients even if it is not possible to control the quality of final dilution due to high level of dilution. It is necessary to describe each phase in the manufacturing process from the starting materials up to the final dilution that enters into the composition of the finished product. Dilution procedures must be performed in accordance with the homeopathic manufacturing methods described in the European Pharmacopoeia or in an official pharmacopoeia of the Member State of the European Union;
- data on the control of the finished product: general requirements for quality apply to homeopathic medicines, and each exception must be justified in detail. It is necessary to identify and determine the content of all the toxicologically relevant ingredients. If identification and determination of the content of the toxicologically relevant ingredients is not possible due to, for example, high degree of dilution in a finished product, the quality has

to be demonstrated by the complete validation of the manufacturing process and dilution process;

- data on stability: it is necessary to demonstrate the stability of the finished medicine. Stability data on homeopathic stocks are generally transferable to dilutions / triturations. If identification and determination of the content of active substance is not possible due to the high degree of dilution, stability data of the pharmaceutical form can be accepted.

Requirements for pharmacological-toxicological documentation relate to the usual data on safety that include data on pharmacodynamics, pharmacokinetics and toxicology.

If some of the data is missing, it is necessary to submit justification documenting acceptable level of safety.

The documentation referred to in paragraph 2 items. 1 and 2 of this Article shall be submitted separately for each pharmaceutical form.

The applicant for enrolment in the Register shall, at the request of the Agency, submit samples of medicines needed for laboratory quality control of medicines.

Article 6

Entering into the Register is done for a period of validity of marketing authorization of a medicine.

Decision on entering into a Register contains, inter alia, name of the homeopathic stock and degree of dilution.

Article 7

The Agency may reject the application for entering into the Register, if, in addition to conditions prescribed by the Law, conditions from Articles 4 and 5 of this Rulebook are not fulfilled.

Article 8

A person at whose request a homeopathic medicine was entered into the Register (hereinafter: holder of Registration) may submit application for amendment to the registration.

The holder of Registration reports to the Agency each amendment to the documents based on which the homeopathic medicine was entered in the Register, as well as the causal change in the patient information leaflet, if applicable.

Along with the application for amendment to the registration, the holder of Registration, in addition to the data referred to in Article 3 of this Rulebook, shall submit data on the number and the date of first entry in the Register and the latest renewal (if applicable), with documentation relating to the amendment.

Article 9

After the expiry of the period of registration, holder of Registration shall apply for the renewal of the entering in the Register.

Along with the application for renewal to the registration, the holder of Registration, in addition to the data referred to in Article 3 of this Rulebook, shall submit data on the number and the date of first entry in the Register and latest renewal (if applicable), with documentation relating to the renewal.

An applicant for renewal of registration shall, at the request of the Agency, submit samples of medicines needed for laboratory quality control of a medicine.

Article10

The documentation referred to in Article 9 paragraph 2 of this Rulebook, shall contain:

1) updated administrative data from Article 4 of this Rulebook;

2) chronological list of approved and submitted amendments during the validity period of entering in the Register;

3) review the data on the safety of homeopathic medicine in the past five years.

Article11

Removing homeopathic medicine from the Register is done at the request of the holder of Registration, or in case that the Agency determines that:

1) the validity period of entry in the Register expired, and no application for renewal was submitted;

2) the benefit-risk ratio is not favorable in the prescribed conditions of use;

3) qualitative or quantitative composition of the medicine does not match the declared composition;

4) the marketed medicine does not comply with the terms of the Decision on entering in the Register;

5) the Decision on entering in the Register was issued on the basis of incomplete and inaccurate data, or, if the data is not amended in accordance with the Law and the regulations adopted for its implementation;

6) the holder of Registration no longer meets the prescribed requirements;

7) the medicine is placed onto the market contrary to the provisions of the Law and regulations adopted for its implementation;

8) the medicine was not marketed in Montenegro three years from the date of issuance of the Decision on entering in the Register, or that a medicine, after issuance of the Decision on entering in the Register, was marketed in Montenegro for a certain period, but after that period, it was not marketed in Montenegro for three consecutive years.

Article 12

Labeling of homeopathic medicines is done in accordance with special regulations.

Article 13

This Rulebook shall enter into force on the eighth day of its publication in the "Official Gazette of Montenegro".

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Acting Minister of Health
Dr Suad Numanović, m.p.
Minister for Human and Minority Rights