MINISTRY OF HEALTH AND SOCIAL WELFARE

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Pursuant to Article 19, paragraph 7 of the Medicinal Products Act (Official Gazette 71/07 and 45/09), the Minister for Health and Welfare hereby issues the

ORDINANCE

ON THE MARKETING, LABELLING AND ADVERTISING OF TRADITIONAL HERBAL MEDICINAL PRODUCTS

I. GENERAL PROVISIONS

Article 1

This Ordinance lays down the procedure, form and content of documents for the issuance of marketing authorisation for traditional herbal medicinal products, necessary evidence of medical use for a period of 30 years, and the rules for labelling and advertising traditional herbal medicinal products.

The provisions of the Medicinal Products Act (Official Gazette 71/07 and 45/09, hereinafter: the Act), provisions of the Ordinance on the procedure and manner of granting marketing authorisations for medicinal products (Official Gazette 113/08 and 155/09) and the Ordinance on special conditions for placement of medicinal products holding marketing authorisation in European Union Member States on the market of the Republic of Croatia (Official Gazette 10/08), and other subordinate legislation adopted pursuant to the Act shall apply appropriately to traditional herbal medicinal products unless otherwise prescribed by this Ordinance.

Article 2

Individual terms shall have the following meaning in the sense of this Ordinance:

1. The procedure for granting marketing authorisation for a traditional herbal medicinal product is the simplified procedure for granting marketing authorisation for a traditional herbal medicinal products, with regard to the content of documentations on safe use and efficacy of a medicinal product (hereinafter: registration of a traditional herbal medicinal product).
2. The Committee for Herbal Medicinal Products (HMPC; hereinafter: Committee) of the European Medicines Agency is a committee comprised of experts in the field of herbal medicinal products that prepares the draft Community list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products (hereinafter: Community List) and the Community herbal monographs (hereinafter: Community monographs).
3. The Community List is a list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products, with information on

indications, strengths, dosage, application and other information necessary for the safe use of traditional herbal medicinal products.

4. The Community monograph is a summary of the scientific opinion of the Committee based on an assessment of the available scientific data, or on the historical use of the product in the European Union. The Community monograph contains a summary of the pharmaceutical, clinical and pharmacological properties of the herbal medicinal product in question, and is used in the procedure for granting marketing authorisation of an herbal medicinal product pursuant to Article 15, item b) of the Act and/or for registration of a traditional herbal medicinal product pursuant to Article 19 of the Act.

II. REQUIREMENTS FOR TRADITIONAL HERBAL MEDICINAL PRODUCTS

Article 3

Traditional herbal medicinal products must meet the following special requirements:

1. they have indications appropriate exclusively to traditional herbal medicinal products which, due to their content and intended use, may be used without a doctor's supervision;
2. they are intended for use exclusively in accordance with the set strength and dosage;
3. they are intended for external or oral use or for inhalation;
4. they have a period of traditional use pursuant to Article 5 of this Ordinance;
5. there must be sufficient information about the traditional use of the medicinal product, in particular, proof that the medicinal product is not harmful under the specific conditions of use and that the pharmacological effects or efficacy of the medicinal product are likely based on the long term use and experience.

The external use from paragraph 1, point 3 of this Article includes use on skin, the mucous membranes of the mouth and nose, rectum or vagina, the outer ear canal and ocular use, under the condition that this primarily refers to local application and that there are no barriers with regard to the safe use of the medicinal product.

Traditional herbal medicinal products may contain vitamins and minerals, if there is existing documented evidence on their safe use, and under the condition that their activity facilitates the activity of the herbal active compounds contained within with regard to the labelled indications.

Traditional herbal medicinal products shall not be considered products containing chemically defined active compounds (synthetic compounds or compounds isolated from herbal materials, such as camphor, menthol, cineol, etc.) or compounds of biological or animal origin (e.g. fish oil, bee products, etc.).

Article 4

The provisions of this Ordinance shall not apply if the Agency for Medicinal Products and Medical Devices (hereinafter: the Agency) should establish during the registration procedure of the traditional herbal medicinal product if the medicinal product meets the requirements from Article 15, point b), Article 107 or Article 108 of the Act for the marketing of a medicinal product or a homeopathic product.

Article 5

For the purpose of establishing the period of traditional use, the applicant is obliged to submit bibliographic evidence or expert evidence that the traditional herbal medicinal product or identical medicinal product thereto has been in medicinal use for a minimum of 30 years from the data of submission of the application, including a minimum period of use of 15 years in the European Union.

The body competent for medicinal products in the European Union Member States may request the opinion of the Committee on the appropriateness of the evidence of long-term use of the medicinal herbal product or identical product, and in doing so much submit the accompanying documentation with its request.

Use of the medicinal product from paragraph 1 of this Article shall be proven in the case when the marketing of the product is not based on a specific authorisation procedure, and when the number or quantity of medicinal product ingredients has been reduced in that period.

If the medicinal product has been in use in the European Union for less than 15 years, and is appropriate for registration as a traditional herbal medicinal product, the European Union Member State in which the application for registration of the traditional herbal medicinal product was submitted shall forward the case to the Committee with the accompanying documentation. The Committee shall consider whether the remaining requirements for registration of the traditional herbal medicinal product have been fully met. If the Committee assesses that the application is founded, it shall draw up a Community monograph, which the European Union Member State shall consider in making the final decision on the application.

III. REGISTRATION PROCEDURE FOR TRADITIONAL HERBAL MEDICINAL PRODUCTS

Article 6

A traditional herbal medicinal product may only be marketed in the Republic of Croatia pursuant to the decision on the registration of the traditional herbal medicinal product.

The registration procedure for a traditional herbal medicinal product shall be initiated by means of a written application submitted to the Agency pursuant to the provisions of the Act and ordinances.

The application for registration of a traditional herbal medicinal product is submitted by a legal person seated in the Republic of Croatia that is:

– the manufacturer responsible for its quality, safe use and efficacy, independent of whether it produced the medicinal product itself or on behalf of another party;

– authorised representative of the foreign manufacturer responsible for its quality, safe use and efficacy, independent of whether it produced the medicinal product itself or on behalf of another party, or the authorised representative with the responsible person of the marketing authorisation holder for the medicinal product in the European Union.

For a traditional herbal medicinal product that does not have marketing authorisation in any country, the registration application may only be submitted by a manufacturer seated in the Republic of Croatia from paragraph 3, subparagraph 1 of this Article.

Article 7

The application must submit documentation along with the application for the registration of a traditional herbal medicinal product containing the following data and documents:

a) name and address of the applicant and manufacturer;

b) name of the medicinal product;

c) qualitative and quantitative composition of all ingredients of the medicinal product with the international non-protected name (INN) proposed by the World Health Organisation, if such a name exists, or a listing of another appropriate name that, for an herbal compound, must include the scientific name of the plan (genus, species, subspecies, authority) and the part of the plant used, and for plant preparations must additional contain the ratio of herbal compounds to the preparation and extraction solvent(s);

d) description of the production process;

e) therapeutic indications, counter-indications and side effects;

f) dosage, pharmaceutical form, manner and application route and expected period of validity;

g) reasons for which special precautionary measures should be taking in the keeping of the medicinal product, its administration to patients, and disposal, with a listing of all possible dangers the medicinal product represents to the environment;

h) description of the procedure the manufacturer uses for the purpose of quality assessment (qualitative and quantitative analysis of active and auxiliary compounds, medicinal product, special testing);

i) results of pharmaceutical testing (physicochemical, biological and/or microbiological testing);

j) summary of product characteristics, other than data from Article 46, point 5 of the Act, proposed internal and external labelling and instructions;

k) manufacturer's production license, exceptionally confirmation of the implementation of good manufacturing practices issued by the competent body of the European Union;

l) information on the granting of a marketing authorisation in a European Union Member State or other country, reasons for rejecting of issuance of a marketing authorisation or revocation of an authorisation within or outside the European Union and the reasons for such a decision;

m) bibliographic evidence or expert evidence that the traditional herbal medicinal product or identical product thereto has been in use for a minimum of 30 years from the date of submission of the application, of which 15 years in the European Union, including information on the traditional area of use, traditional indications, strength, dosage, manner and duration of use;

n) bibliographic overview of data on the safety of use, together with an expert report and, at the request of the Agency, additional information necessary to assess the safe use of the medicinal product (e.g. information on genotoxicity);

o) proof that the applicant has at its disposal a qualified person responsible for pharmacovigilance and that it meets the requirements relating to reporting on all suspicions of adverse effects observed either in the Republic of Croatia or in any other country.

If the traditional herbal medicinal product contains a combination of active compounds, the applicant shall be obliged to submit information from Article 3, paragraph 1, point 5 of this Ordinance for the combination in question, and information on individual active compounds if they are not sufficiently known.

The documentation on the results of pharmaceutical testing should contain a detailed expert report that must objectively and critically assess the data on the quality of the medicinal product.

The applicant is obliged to submit the expert statement from paragraph 3 of this Article in which the signature and date confirm the appropriate qualifications of the expert compiling the report on individual parts of the documentation.

Article 8

If the application for registration of the traditional herbal medicinal product pertains to an herbal compound, preparation or combination thereof that is included on the Community List, the applicant shall not need to submit the information from Article 7, paragraph 1, subparagraph l), m) and n) of this Ordinance.

If the herbal compound, preparation or combination thereof is no longer included on the Community List, the approval for registration of the traditional herbal medicinal product granted pursuant to paragraph 1 of this Article shall be revoked unless the authorisation holder submits all the information and documents required under Article 7 of this Ordinance within a deadline of three months.

Article 9

The applicant is required to enclose with the application for registration of the traditional herbal medicinal product the documentation on the traditional herbal medicinal product in the form of the Common Technical Document (hereinafter: CTD) pursuant to the provisions of the Ordinance on the procedure and manner of issuing marketing authorisation for a medicinal product.

The applicant shall submit the documentation from paragraph 1 of this Article purusant to the Addendum prescribing special requirements and the content of documentation for the

traditional herbal medicinal product, which is contained in the appendix to this Ordinance and which forms its integral part.

Article 10

The registration procedure for the traditional herbal medicinal product shall be carried out according to the national procedure for the issuance of marketing authorisation for a medicinal product in the Republic of Croatia pursuant to the provisions of the Ordinance on the procedure and manner of issuing marketing authorisation for medicinal products.

Exceptionally from the provisions of paragraph 1 of this Article, when the Committee has adopted the Community monograph for an herbal compound or preparation contained within the herbal medicinal product in question, or when the herbal medicinal product contains an herbal compound, preparation or combination thereof from the Community List, the registration procedure for the traditional herbal medicinal product shall be carried out pursuant to the provisions prescribing the procedures for mutual recognition or the decentralised procedure for issuing marketing authorisation for a medicinal product.

Article 11

The registration of the traditional herbal medicinal product shall be denied if the information and documents are not in line with the provisions of Articles 7, 8 and 9 of this Ordinance, if any of the following are established:

- the qualitative and/or quantitative composition is not identical to that declared;
- the indications are not in accordance with Article 3, paragraph 1, point 1 of this Ordinance;
- the product can be harmful in the usual conditions of use;
- information on traditional use are not sufficient, particularly if the pharmacological effects or efficacy are not likely based on the long-term use and experience;
- the pharmaceutical quality is not satisfactorily portrayed.

In the case from paragraph 1 of this Article, the Agency is obliged to inform the European Commission and at the request of another competent body on the denial of the registration of a traditional herbal medicinal product and of the reasons for such a decision.

Article 12

When an herbal compound, preparation or combination thereof is included on the Community List, or following adoption of its Community monograph, the authorisation holder for the traditional herbal medicinal product containing the said active compound is obliged to harmonise the medicinal product documentation (summary of product characteristics, patient information and labelling) with the said documents and submit to the Agency the application for approval of amendments to the registration.

Article 13

The labelling and patient information for the traditional herbal medicinal product, with the information and requirements from Article 41 to 47 of the Act and Articles 13 to 17 of the Ordinance on the procedure and manner of granting marketing authorisation for a medicinal product, must contain the following claims:

- that the product is a traditional herbal medicinal product for use for the listed indications based on experience from long-term use, and
- that the patient should consult a doctor or pharmacist if their symptoms do not cease during the course of use of the medicinal product, or in the case of appearance of adverse reactions listed in the patient information.

The Agency may request the registration holder to list the types of traditional use of the medicinal product in question in the labelling and patient information.

Article 14

When advertising the traditional herbal medicinal product, in addition to the requirements from Articles 82 to 86 of the Act and the Ordinance on the manner of advertising medicinal products and homeopathic products (Official Gazette 118/09 and 140/09), the following message must be contained within the advertisement or notice: "Traditional herbal medicinal product for use for the listed indications based on the experience of long-term use".

Article 15

Herbal products meeting the definition of the traditional herbal medicinal product from Article 2, point 20 of the Act, and which are marketed as of the date of coming of this Ordinance into effect, must be registered pursuant to the provisions of this Ordinance within two years of the date of coming of this Ordinance into effect.

Article 16

This Ordinance shall enter into force on the eighth day from its publication in the Official Gazette, with the exception of the provisions of Article 5, paragraphs 2 and 4, Article 10 and Article 11, paragraph 2 of this Ordinance, which shall come into effect as of the date of accession of the Republic of Croatia to the European Union.

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