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Committee on Herbal Medicinal Products (HMPC)

Opinion of the HMPC on a European Union herbal monograph on *Cimicifuga racemosa* (L.) Nutt., rhizoma

Opinion

The HMPC, in accordance with Article 16h(3) of Directive 2001/83/EC and as set out in the appended assessment report, establishes, by a majority of 20 out of 25 votes a European Union herbal monograph on *Cimicifuga racemosa* (L.) Nutt., rhizoma which is set out in Annex I.

The divergent positions are appended to this opinion.

The Norwegian HMPC member does agree with the above-mentioned recommendation of the HMPC.

This opinion is forwarded to Member States, to Iceland and Norway, together with its Annex I and appendices.

The European Union herbal monograph and assessment report will be published on the European Medicines Agency website. They replace those adopted on 25 November 2010.

London, 27 March 2018

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Annex I: European Union herbal monograph (EMA/HMPC/48745/2017)

Appendix I: Assessment report (EMA/HMPC/48744/2017)

Appendix II: Divergent positions

The member of the HMPC mentioned below did not agree with the HMPC's opinion for the following reason:

"Products manufactured from *Cimicifuga racemosa* (L.) Nutt. rhizome have been reported to exert toxic liver effects, sometimes life-threatening, that have been characterized and documented in humans and experimentally in rats. Histologically the reactions have been identical to autoimmune hepatitis and similar in humans and rats. Warnings in the monograph concerning liver symptoms do not exclude risk to the patient, as liver diseases usually induce symptoms only at late stage of the disease, when liver damage often is irreversible. In some reported cases, liver damage developed very quickly, within days.

As the proposed indication, i.e. relief of menopausal complaints such as hot flushes and profuse sweating, is not a life-threatening disease, any risk of life-threatening adverse reactions is not regarded acceptable. Therefore, the benefit to risk ratio is deemed negative."

Eeva Sofia Leinonen, HMPC Member from Finland

London, 27 March 2018

The member of the HMPC mentioned below did not agree with the HMPC's opinion for the following reason:

I do not support the proposed monograph for Cimicifugae rhizoma.

The data provided are considered insufficient to support a well-established use indication for Cimicifugae rhizome as a 'herbal medicinal product for the relief of menstrual complaints'.

The clinical trials are not considered of adequate quality and Cimicifugae rhizoma is not considered to be scientifically proven to have recognised efficacy as required by Article 10a and the Annex of Directive 2001/83/EC, as amended.

Furthermore, there are insufficient genotoxicity data to support well-established use.

Rachel Cox, HMPC Member from Ireland

London, 27 March 2018

The member of the HMPC mentioned below did not agree with the HMPC's opinion for the following reason:

I do not agree with the HMPC's opinion Community herbal monograph on *Cimicifuga racemosa* (L.) Nutt., rhizoma for the following reasons:

The scientific data provided are insufficient to consider *Cimicifuga racemosa* (L.) Nutt., rhizoma as well established treatment for the relief of menopausal complaints such as hot flushes and profuse sweating.

Clinical data for the Dry extract (DER 6-11:1), extraction solvent propan-2-ol 40% (V/V) are conflicting and do not provide a sound proof of efficacy in the improvement of the above mentioned climateric symptoms.

For the Dry extract (DER 4.5-8.5:1), extraction solvent ethanol 60% (V/V) a recent RCT by Schellenberg et al., 2012, even with some limitations, provides some evidence of an effective use of *Cimicifuga racemosa* (L.) Nutt., rhizoma in pre-, early and post-menopausal patients suffering from menopausal syndrome; however, the duration of the study is limited to three months and there is no clear demonstration that the therapeutic effect could be maintained up to six months as reported in the monograph.

The posology reported in the monograph for the Dry extract (DER 5-10:1), extraction solvent ethanol 58% (V/V) is derived from the study by Wuttke et al. 2003 and 2006, but this study presents deficiences in clinical methodology (i.e. small sample size and many protocol deviations) and conflicting results. Furthermore, there is no clear demonstration that the therapeutic effect could be maintained up to six months as reported in the monograph.

Alessandro Assisi, HMPC Member from Italy

London, 27 March 2018

The member of the HMPC mentioned below did not agree with the HMPC's opinion for the following reason:

I do not support the revised EU Herbal monograph for Cimicifuga racemosa, rhizoma.

For a well-established use (art. 10a) assessment it should be taken into account that the scientific data should be similar to those for a full application as in article 8.3, with the difference that those data may be replaced by published scientific literature, demonstrating 10 years of use with recognised efficacy and an acceptable level of safety.

The benefit/risk is considered negative for the well-established use of Cimicifugae rhizoma. The published data are considered of insufficient quality for the demonstration of efficacy for menopauzal related symptoms, including for hot flushes. For this indication proof of efficacy should respect the recommendations of the guideline on HRT (EMA/CHMP/021/97).

Emiel van Galen, HMPC Member from The Netherlands

London, 27 March 2018

The member of the HMPC mentioned below did not agree with the HMPC's opinion for the following reason:

The United Kingdom does not support the proposed monograph for Cimicifugae rhizoma.

The data provided are considered insufficient to support a well-established use indication for Cimicifugae rhizome as a 'herbal medicinal product for the relief of menstrual complaints'.

The clinical trials are not considered of adequate quality and Cimicifugae rhizome is not considered to be scientifically proven to have recognised efficacy as required by Article 10a and the Annex of Directive 2001/83/EC, as amended.

Furthermore, there are insufficient genotoxicity data to support well-established use.

Linda Anderson, HMPC Member from United Kingdom

London, 27 March 2018