



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee on Herbal Medicinal Products (HMPC)

Overview of comments received on Community herbal monograph on *Juniperus communis* L., pseudo-fructus (EMA/HMPC441929/2008)

This document was valid from 12 November 2009 until 15 March 2023.

on *Juniperus communis* L., pseudo-fructus as released for public consultation on 14 January 2009 until 15 May 2009.

	Organisations and/or individuals
1	Kooperation Phytopharmaka GbR, Germany



Table 2: Discussion of comments

General comments to draft document

Interested party	Comment and Rationale	Outcome
Kooperation Phytopharmaka	<p>In principle welcomes the preparation of the above-mentioned Community herbal monograph. However, we would like to comment on some paragraphs.</p> <p>The reference Schilcher H., Lauschner F. Untersuchungen auf mögliche nephrotoxische Wirkungen von aetherischen Wacholder (Juniperus communis L.) Experientia 1957; 13: 255-256.</p> <p>should be replaced by: Schilcher H., Leuschner F. Untersuchungen auf mögliche nephrotoxische Wirkungen von aetherischem Wacholderöl. Arzneimittel-Forschung/Drug Research 1997; 47(11): 855-858.</p>	<p>Reference has been verified and replaced.</p> <p>Endorsed.</p>

SPECIFIC COMMENTS ON TEXT

Section number and heading	Interested party	Comment and Rationale	Outcome
2. Qualitative and quantitative composition	Kooperation Phytopharmaka	Among the listed herbal preparations, essential oil of juniper berries should be added.	As a separate monograph for juniper oil exists in the European Pharmacopoeia and in line with the HMPC policy, a separate HMPC monograph on juniper oil has been established. Endorsed.
3. Pharmaceutical Form	Kooperation Phytopharmaka	Essential oil of juniper berries should be added	See above. Endorsed.
4.2 Posology, duration of use and method of administration	Kooperation Phytopharmaka	<p>The posology recommended for cone berries in the traditional use indication „to increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary tract complaints” is: To start on day 1 with 5 cone berries, increasing the number every day by 1 coneberry (well chewed) up to 15 cone berries. This corresponds to the recommendation of Sebastian Kneipp.</p> <p>There are further posologies, starting with an initial dosis of 2 g of juniper berries up to 20 g of berries. The posology recommended by the German Commission E of “2 g up to a maximum dosis of 10 g” is based on practical therapeutic experience.</p>	<p>As stated by Kooperation Phytopharmaka, this posology can remain in the monograph.</p> <p>Endorsed.</p> <p>It can be more reliable to express the posology as standardised weight instead of the number of berries. According to several sources, infusions may contain a maximal dose of 10 g cone berries per day. However, this dose cannot be extrapolated directly. The approximate weight of 100 cone berries is 16 g (Schilcher & Heil, 1994). A dose of 10 g would correspond to approximately 60 cone berries. This amount seems quite high.</p>

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		<p>The posology for the essential oil is missing. We propose the following: Calculated from the posology given for the berries as well as on the basis of reports from medical experience the daily dose of essential oil of juniper berries should be 50 to 100 mg.</p>	<p>The content of essential oil in cone berries may vary from 0.5 to 3.42%. When the content of essential oil is high, a daily dose of 10 g corresponds to about 342 mg of essential oil, whereas a maximal daily dose of 100 mg is recommended according to several sources.</p> <p>As a result of these considerations, it was decided to follow the recommendations by Sebastian Kneipp.</p> <p>Not endorsed.</p> <p>See comment above regarding the establishment of a monograph on juniper oil..</p> <p>Endorsed.</p>
4.2 Posology, duration of use and method of administration	Kooperation Phytopharmaka	<p>The restriction of the duration of use to a maximum of 3 weeks without consulting a doctor or a qualified health care practitioner is not justified when the preparation is made from ripe, blue juniper berries. In case of intake of an inappropriately produced essential oil, renal irritation may occur (Schilcher et Heil 1994, Schilcher et Leuschner 1997, Schilcher, Emmrich et Koehler 1993). The renal irritation factor describes the ratio of terpinol-4-ol to the total pinenes which possess renal irritating properties. For further details see the three above-mentioned publications as well as Schilcher, Kammerer et Wegener 2007)</p>	<p>The risk is indeed minimal when respecting the posology.</p> <p>However, the restriction of the duration of use relates to possible hidden pathologies for which the patient must seek professional medical advice. The duration of use according to the posology of Sebastian Kneipp takes 3 weeks. After discussion, the MLWP recommended that patients should seek medical advice if symptoms persist after 2 weeks during the use of the medicinal products.</p> <p>Not endorsed.</p>

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4.4. Special warnings and precautions for use'	Kooperation Phytopharmaka	<p><u>Traditional use</u></p> <p>The draft monograph states that juniper berries should not be used in children and adolescents under 18 years of age. There is no toxicological or any other scientific justification for this restriction (Schilcher et Leuschner 1997, Schilcher et Heil 1994), although tolerability studies in this population have not been performed. It can be assumed that children consume juniper berries to the same extent for food as the adult population.</p> <p>For preparations containing ethanol, the appropriate labelling for ethanol according to the 'Guideline on excipients in the label and package leaflet of medicinal products for human use, should be included.</p>	<p>After discussion the MLWP decided to maintain the age restriction as it is, mainly due to the therapeutic indication.</p> <p>Not endorsed.</p> <p>This warning is already included as a standard paragraph under section '4.4. Special warnings and precautions for use'</p> <p>Endorsed.</p>
4.4. Special warnings and precautions for use'	Kooperation Phytopharmaka	<p>The following warnings:</p> <p>"If complaints of symptoms such as fever, dysuria, spasms or blood in the urine occur during the use of the medicinal product, a doctor or a qualified health care professional should be consulted." as well as "Concomitant treatment with synthetic diuretics is not recommended."</p> <p>are only applicable to cases of intake of inappropriately produced essential oil (Schilcher, Emmrich et Koehler 1993). It should not be applicable to juniper berries which conform to the specification of the German Pharmacopoeia (DAB) requiring e.g. that the herbal drug may not contain unripe berries.</p>	<p>We agree that the toxicity of juniper berries has been overestimated in literature.</p> <p>On the other hand, these warnings have been included in other similar monographs and are more related to uncontrolled pathological conditions due to complications. In such events, patients should seek professional medical advice.</p> <p>Not endorsed.</p>

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4.9 Overdose	Kooperation Phytopharmaka	<p>The draft monograph states that seizures and kidney damage have been reported in individuals who took more than 10 g of Juniper per day or who took high doses of Juniper for longer than 4 weeks.</p> <p>Such reports can not be based on preparations conform to pharmacopoeal standards. According to a critical evaluation of scientific literature between 1844 and 1993 (Schilcher et Heil 1994) they were exclusively caused by the intake of inappropriately produced juniper berry oil (produced from ripe and unripe fruits as well as under co-distillation of juniper needles and juniper wood)</p>	<p>The reporting is indeed rather vague and linked to some websites like: http://www.rxlist.com/juniper/supplements.htm (last visit on 2 July 2009). It cannot be excluded that the oil was contaminated.</p> <p>The first paragraph of 4.9. has been omitted.</p> <p>Endorsed.</p>

References:

Commission E. Monograph: Juniperi fructus (Wacholderbeeren). BAnz. No. 228 of 5.12.1984. List of references.

Schilcher H., Emmrich D., Koehler Chr.. Chromatographischer Vergleich von ätherischen Wacholderölen und deren toxikologischen Bewertung. Pharmazeutische Zeitung Wissenschaft 1993; 138 (3/4): 85-91.

Schilcher H., Heil BM.. Nierentoxizität von Wacholderbeerzubereitungen. Zeitschrift für Phytotherapie 1994; 15: 205-213.

Schilcher H, Kammerer S, Wegener T. In: Leitfaden Phytotherapie. 3.Aufl.2007 Elsevier, Urban und Fischer Verlag, 276

Schilcher H., Leuschner F. Untersuchungen auf mögliche nephrotoxische Wirkungen von aetherischem Wacholderöl. Arzneimittel-Forschung/Drug Research 1997; 47(11): 855-858.