

7 July 2015  
EMA/HMPC/268114/2015  
Committee on Herbal Medicinal Products (HMPC)

## Overview of comments received on European Union herbal monograph on *Carum carvi* L., fructus (EMA/HMPC/715092/2013)

**Table 1:** Organisations and/or individuals that commented on the draft European Union herbal monograph on *Carum carvi* L., fructus as released for public consultation on 24 November 2014 until 15 March 2015.

	Organisations and/or individuals
1	Association of the European Self-Medication Industry (AESGP)
2	Kooperation Phytopharmaka (KOOP Phyto)



**Table 2:** Discussion of comments

Comments on the assessment report were also submitted. The Assessment Report is summarising the data which contribute to establishing a harmonised view in a European Union Monograph. As mentioned in the disclaimer of the draft assessment report supporting the monograph, the focus of the public consultation is not to comment on the assessment report. If suggestions for changes of the monographs are justified and substantiated with references, the suggestions are discussed and, if finally endorsed, the relevant documents are amended.

### **General comments to draft document**

Interested party	Comment and Rationale	Outcome
AESGP	<p>AESGP welcomes the development of the above-mentioned Community herbal monograph which, by providing harmonised assessment criteria for Carum-containing products, should facilitate mutual recognition in Europe.</p> <p>It is appreciated that this very important plant is now covered by a monograph, for which therapeutic usefulness has been known since Antiquity and has never been questioned since then. The therapeutic indication "for the symptomatic relief of digestive disorders" is also appreciated.</p> <p>We note that one common assessment report was prepared for Carvi fructus and Carvi aetheroleum. Nevertheless it needs to be emphasised that, similarly to the situation in camomile flowers, mentha leaves, or fennel fruits, there are very basic differences between the pharmaceutical and therapeutic profiles of the herbal drug and extracts thereof, and the essential oil obtained from it. Indeed, the herbal drug as well as the extracts thereof only have a minor content of essential oil (also due to the limited efficacy of especially an aqueous extraction), but contain a considerable number of other components with known pharmacological action relevant to the indication (cf. Wegener and Wagner 2006).</p> <p>As there is documented therapeutic experience of the use of caraway extracts in children also below 12 years, and there are also recommendations of the use in</p>	The use in children is commented below.

Interested party	Comment and Rationale	Outcome
	this age group in textbooks, it seems justified to also include children below 12 years into the posology, preferentially from 4 years of age on, as is the case in fennel fruits (see below for details).	
KOOP Phyto	<p>The monograph on <i>Carum carvi</i> L., fructus gives good information on the therapeutic use of this drug and preparations thereof in the indication "for the symptomatic relief of digestive disorders".</p> <p>KOOP Phyto would like to comment on some points. It is good that the monographs on Carvi fructus and Carvi aetheroleum are separated, as there are large differences between these both preparations as the herbal drug as well as its extracts thereof contain very limited amounts of essential oil, while other phytochemical components are much more predominant, so that its clinical, pharmacological and toxicological properties are, as pointed out in the assessment report, are very different (see also: Wegener and Wagner 2006).</p> <p>While many sections of the monograph are highly appreciated in general, it seems necessary to question the age limit of 12 years for Carvi fructus, based on the data and the clinical experience mentioned below, and proposing a lower age limit, e.g. in the range of 3 or 4 years, as in the monographs of certain other drugs like Marshmallow root or Fennel fruit.</p>	See comments below.

## Specific comments on text

Section number and heading	Interested party	Comment and Rationale	Outcome
4.2. Posology and method of administration	AESGP	<p>"The use in children 12 years of age is not recommended" – should presumably read "... under 12 years of age ...".</p> <p>It seems justified to also include children below 12 years of age to the posology, as is the case e.g. in fennel fruits. There indeed is documented use of caraway fruits also in children, as compiled by Kooperation Phytopharmaka in its book "Kinderdosierungen von Phytopharmaka" from 2002.</p> <p>For a combination of camomile flower, caraway fruit and other components, 1551 prescriptions/month by paediatric physicians in children below 12 years were registered, for another preparation containing bitter candy tuft, caraway fruits and others, 263 prescriptions, and for a third preparation containing chiretta herba, caraway fruits and others, 26 prescriptions.</p> <p>Given that these figures are prescriptions per month, this provides a rather high body of experience. Despite the fact that these figures are for combination preparations with carvi, they attest of the safety of use in children.</p> <p>In the same book, the following recommended doses of caraway drug are reported:</p> <ul style="list-style-type: none"> <li>0-1 year: 1 g</li> <li>&gt; 1-4 years: 1-2 g</li> <li>&gt; 4-10 years: 1-4 g</li> <li>&gt; 10-16 years: 2-6 g</li> </ul>	<p>Not endorsed. The oral use in children under 12 years of age has not been established due to lack of adequate data. The provided references refer to combination products. In addition the provided references are published in 2002 and 2008. Thus, traditional medicinal use according to Directive 2004/24/EC is not considered fulfilled for oral administration of caraway fruit to children under 12 years of age.</p>

Section number and heading	Interested party	Comment and Rationale	Outcome
		<p>The latter dose is identical to that in this draft monograph.</p> <p>This dose scheme is also recommended in a textbook of herbal medicine for children (Bühring et al. 2008).</p> <p>Therefore we propose to change the posology and add the following (as is the case in sweet fennel fruits):</p> <p><i>"Children between 4 and 12 years of age</i></p> <p><i>Average daily dose</i></p> <p><i>1-4 g of the herbal substance or comminuted herbal substance in 150 ml of boiling water as a herbal infusion 1-3 times daily, for short-term use in mild transitory symptoms only (less than one week)</i></p> <p><i>The use is not recommended in children under 4 years of age (see section 4.4 Special warnings and precautions for use)".</i></p>	
4.2. Posology and method of administration	KOOP Phyto	<p>There is the sentence "The use in children 12 years of age is not recommended" – which is presumably intended to read like "The use in children of 12 years of age is not recommended"</p> <p>With regard to the age limit:</p> <p>In the book "Kinderdosierungen von Phytopharmaka" of Kooperation Phytopharmaka, Bonn, Germany (2002), data on the prescriptions (per month) by paediatric physicians in children below 12 years of age are documented for combination preparations containing caraway fruit extracts:</p> <p>For a preparation containing extracts from bitter candy tuft, caraway fruits and other herbal drugs, 263 prescriptions per month are documented in this book. For this combination (Iberogast), there is also documented therapeutic experience from more than 40.000 children (NIS and retrospective</p>	<p>Not endorsed. The oral use in children under 12 years of age has not been established due to lack of adequate data. The provided references refer to combination products. In addition the provided references are published in 2002 and 2006. Thus, traditional medicinal use according to Directive 2004/24/EC is not considered fulfilled for oral administration of caraway fruit to children under 12 years of age.</p>

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		<p>evaluations) (Ottillinger <i>et al.</i> 2013).</p> <p>For another combination containing camomile flower, caraway fruit and other components, 1551 prescriptions/month are listed, and for a further preparation containing chiretta herbs, caraway fruits and others, 26 prescriptions/month are listed.</p> <p>This book contains also information on recommended daily doses of caraway drug:</p> <p>0 to 1 year of age: 1 g</p> <p>more than 1 to 4 years of age: 1-2 g</p> <p>more than 4 to 10 years of age: 1-4 g</p> <p>more than 10 to 16 years of age: 2-6 g</p> <p>The latter dose is similar to that in this monograph draft.</p> <p>In a textbook of herbal medicine for children mentioned above (Bühring <i>et al.</i> 2008) the same dose scheme is recommended.</p> <p>In a further textbook (Schilcher and Dorsch 2006), a combination of Anisi fructus, Foeniculi fructus and Carvi fructus (1:1:1) ("AFK") is recommended as an infusion for use in all age groups.</p> <p>Therefore, there is a broad body of experience supporting the safe use of Carvi fructus also in children below 12 years of age. Therefore an age limit of 4 years as in Foeniculi fructus or even 3 years as in Altheae radix could seem adequate, in case that an adequate dosing scheme is used.</p> <p>Such a dosing scheme for children below 12 years could look as follows (see e.g. the monographs on Foeniculi fructus or Altheae radix for comparison):</p>	

Section number and heading	Interested party	Comment and Rationale	Outcome
		<p>"Children between 4 and 12 years of age, for short term use in mild transitory symptoms only (less than 1 week).</p> <p>Average daily dose</p> <p>1-4 g of the herbal substance or comminuted herbal substance in 150 ml of boiling water as an herbal infusion in 3 divided doses.</p> <p>Children of 3 years of age, for short term use in mild transitory symptoms only (less than 1 week):</p> <p>Average daily dose</p> <p>1-2 g of the herbal substance or comminuted herbal substance in 150 ml of boiling water as a herbal infusion in 3 divided doses.</p> <p>The use is not recommended in children under 3 years of age.</p>	
4.4. Special warnings and precautions for use	AESGP	<p><i>In accordance with our comments to Section 4.2 above, the first sentence should be changed to: "The use in children and adolescents under 12 4 years of age has not been established due to lack of adequate data."</i></p>	Not endorsed. See comments above.
4.4. Special warnings and precautions of use	KOOP Phyto	<p>There is written: The use in children and adolescents under 12 years of age has not been established due to lack of adequate data.</p> <p>This text could be consequently modified to:</p> <p>The use in children and adolescents under 4 years (or 3 years) of age has not been established due to lack of adequate data.</p>	Not endorsed. See comments above.

References (not contained in EMA/HMPC/242200/2014 and therefore supplied as copies):

- Bühring U, Ell-Beiser H, Girsch M, Heilpflanzen in der Kinderheilkunde. Das Praxis-Lehrbuch. Sonntag-Verlag, Stuttgart, Germany, 2008: 93-4

2. Kooperation Phytopharmaka (Ed.), Kinderdosierungen von Phytopharmaka. 3rd ed., Bonn, Germany, 2002: 51-52: 194-199
3. Ottillinger B, Storr M, Malfertheiner P, Allescher HD. STW 5 (Iberogast) – a safe and effective standard in the treatment of functional gastrointestinal disorders. Wien Med Wochenschr 2013, 163: 66-72 (open access: <http://rd.springer.com/article/10.1007%2Fs10354-012-0169-x#>)
4. Schilcher H., Dorsch W.: Phytotherapie in der Kinderheilkunde. Ein Handbuch für Ärzte und Apotheker. Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart, Germany, 2006: 55-56
5. Wegener T, Wagner H, The active components and the pharmacological multi-target principle of STW 5 (Iberogast). Phytomedicine 2006, 13 (Suppl 5): 20-35 (open access <http://www.sciencedirect.com/science/journal/09447113/13/supp/S1>)