



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 November 2012
EMA/HMPC/196724/2012
Committee on Herbal Medicinal Products (HMPC)

Overview of comments received on Community herbal monograph on *Cucurbita pepo* L, semen (EMA/HMPC/136024/2010)

Table 1: Organisations and/or individuals that commented on the draft Community herbal monograph on *Cucurbita pepo* L, semen as released for public consultation on 15 November 2011 until 15 February 2012.

	Organisations and/or individuals
1	Association of the European Self-Medication Industry (AESGP)
2	European Scientific Cooperative on Phytotherapy (ESCOP)
3	Frutarom Switzerland Ltd
4	HerbResearch Germany



Table 2: Discussion of comments

General comments to draft document

Interested party	Comment and Rationale	Outcome
AESGP	AESGP in principle welcomes the development of the above-mentioned Community herbal monograph which, by providing harmonised assessment criteria for cucurbita-containing products, should facilitate mutual recognition in Europe.	Rapporteurs thank for the appreciation of the work on assessment report and monograph.
ESCOP	We welcome the preparation of a Community draft monograph on Pumpkin seed and would like to comment as follows.	Rapporteurs thank for the appreciation of the work on assessment report and monograph.
HerbResearch	We would like to turn your attention to an additional extract preparations commercially available on the Austrian market and potentially eligible for traditional herbal medicinal product registration.	See below

SPECIFIC COMMENTS ON TEXT

Section number and heading	Interested party	Comment and Rationale	Outcome
2. Qualitative and quantitative composition	HerbResearch Germany	<p>The draft monograph mentions as preparation c) a dry extract (15-30:1), extraction solvent ethanol 60% v/v.</p> <p>There is another, albeit similar extract form available in Austria: Dry extract 15-25:1 (DEV native 21-36:1), ethanol 60% v/v.</p> <p>Reference:</p> <p>Specification of the manufacturer Frutarom (formerly Flaxmann)</p> <p>This extract has been marketed in food supplements and dietary products for specific medicinal purposes, and can be</p>	<p>Not endorsed.</p> <p>The mentioned product is on the market since 1994 (18 years). In the absence of evidence for 30 years of medicinal use the proposed herbal preparation cannot be included in the monograph.</p>

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		<p>traced back to at least the year 1994.</p> <p>References:</p> <ul style="list-style-type: none"> - Scans of packaging materials - Scans of regulatory notifications demonstrating the availability of the products - Sales figures <p>Although the extract composition is similar to preparation c), we think this alternative formulation should also be included in the list of preparations, for two reasons:</p> <ul style="list-style-type: none"> -The available products also included monopreparations, not only combinations as listed for Austria in the Assessment Report. - The dose recommendation differed from the statement of the draft monograph (see below). <p>We suggest the following addition:</p> <p>x) Dry extract (15-25:1), extraction solvent ethanol 60% v/v.</p>	
4.1 Therapeutic indications	AESGP	<p>We highly appreciate the wording proposed for the therapeutic indications, in particular the option to treat symptoms of benign prostatic hyperplasia (BPH) after serious conditions have been excluded by a medical doctor.</p> <p>From our point of view the wording proposed for the indications corresponds to current scientific data and takes into account the option to treat more serious conditions such as BPH symptoms after medical consultation and diagnosis.</p>	Rapporteurs thank for the appreciation of the work on assessment report and monograph.
4.1. Therapeutic indications	ESCOP	<p>We welcome the indications proposed in the HMPC draft monograph because e.g. the treatment of symptoms of BPH (which is a more serious condition) will be permitted in self-medication after consultation of a medical doctor.</p>	Rapporteurs thank for the appreciation of the work on assessment report and monograph.

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4.2. posology and method of administration	Frutarom Switzerland Ltd	<p>The dosage recommendation of the dry extract (c) is much lower than that of the herbal preparation (a). We propose to change the dosage of the dry extract, using the average DER of 22.5, to 300 – 900 mg.</p> <p>Frutarom produces a Pumpkin seed extract (DER 15-25: 1) which is being used with a dosage recommendation of 500 mg /day. This extract is being produced since the eighties and used in several products worldwide. Scientific research has shown that the 500 mg dose shows significant results after a defined period of intake.</p>	<p>Not endorsed.</p> <p>The posology in the monograph is based on products which were at least 30 years in medicinal use in the proposed indication. An increase in the posology is not justified by the traditional use.</p> <p>There is no evidence available on 30 years of medicinal use of the mentioned herbal preparation in the EU.</p>
4.2. Posology and method of administration	HerbResearch Germany	<p>For preparation c) the draft monograph states:</p> <p>300-320 mg, divided into 2-3 single doses.</p> <p>The above-cited materials show the availability of the following products and their respective dose recommendations. In all cases the above described Frutarom extract is used:</p> <p>Kürbis Nur eine Tablette täglich Dr. Böhm. Mono-preparation. Marketed as food supplement since at least 1994 (see marketing figures) in pack sizes of 30 and 90 tablets. Dose recommendation: 500 mg (one tablet) once daily.</p> <p>Kürbis Tabletten Dr. Böhm für die Frau. Marketed as dietary food product since at least since 2003 (see regulatory letters) in pack sizes of 30 and 60 tablets. Combination product containing 400 mg of pumpkin extract (see above) and soy extract (30 mg, normalised to 12 mg isoflavones). Dose</p>	<p>Not endorsed.</p> <p>No evidence for 30 years of medicinal use.</p>

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		<p>recommendation 2x1 tablet daily (initially up to 3x1 tablet daily, corresponding to a daily dose of 800-1200 mg pumpkin seed extract.</p> <p>Kürbis nur eine Tablette täglich mit 420 mg Kürbiskernextrakt. Monopreparation (Food supplement) marketed since at least 1996 with 420 mg of the above-mentioned pumpkin extract per tablet. Once daily.</p> <p>Kürbiskern Tabletten mit Brennesselextrakt. Combination product with nettle herb extract as food supplement, marketed at least since 1996.</p> <p>The documents provided and referenced to in the comments to Section 2 suggest an amendment of the dosing recommendation in section 4.2, or otherwise an inclusion of an additional preparation corresponding to the Frutarom extract in section 2, and a corresponding dose recommendation in section 4.2:</p> <p>x) Dry extract</p> <p>500 mg once daily or 800-1200 mg divided in 2-3 doses.</p>	
4.4 Fertility, pregnancy and lactation	AESGP	<p>We suggest taking into consideration that there is a long-term use of pumpkin seeds and fatty oil as food. In some countries the seeds are widely used e.g. in bread, and there is no evidence about any harmful effects.</p>	<p>Sections 4.4 and 4.6 have been revised as follows:</p> <p>Section 4.4.</p> <p>“The use in children and adolescents under 18 years of age and the use in pregnant women (see also section 4.6.) are not recommended because lower urinary</p>

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			<p>tract symptoms in these populations require medical supervision."</p> <p>Section 4.6</p> <p>"Safety during pregnancy and lactation has not been established for pumpkin extracts. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.</p> <p>No concern has arisen about any malformation in humans, following the consumption of pumpkin seeds and fatty oil. Can be used during pregnancy and lactation if clinically needed."</p>