



European Medicines Agency
Evaluation of Medicines for Human Use

London, 4 September 2008
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**OVERVIEW OF COMMENTS RECEIVED ON
'COMMUNITY HERBAL MONOGRAPH ON AVENA SATIVA L., HERBA'
(EMEA/HMPC/202966/2007)**

Table 1: Organisations providing comments on 'Community herbal monograph on *Avena sativa* L., herba' as released for consultation on 31 October 2007 until 15 February 2008

Organisation	
1.	The Association of the European Self-Medication Industry (AESGP)
2.	Kooperation Phytopharmaka, Germany

GENERAL COMMENTS	COMMENT AND RATIONALE	RAPPORTEUR'S COMMENTS
<p>2. QUALITATIVE AND QUANTITATIVE COMPOSITION</p> <p>With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended. <i>Avena sativa</i> L., herba (oat herb)</p> <p>i) Herbal substance Dried aerial parts harvested before flowering</p> <p>ii) Herbal preparations</p> <ul style="list-style-type: none"> - Comminuted herbal substance as an infusion - Liquid extract (4-6 5:1; water or ethanol 45 15-50 % v/v) prepared from the fresh aerial parts of the plant harvested during the flowering period herbal substance <p>iii) Dry extracts corresponding to extracts mentioned under ii)</p> <p>iv) Expressed juice from the fresh herb</p>	<ul style="list-style-type: none"> - The infusion of green oat herb is commonly prepared using boiling water (Hagers Handbuch, cf. HMPC list of references). Aqueous extracts should thus be included in the monograph. - Several compositions of solvents for extraction were tested for their activity during the bioactivity-based development of the green oat extract. The activity profiles showed that 15-50% ethanolic extracts exert an inhibitory effect on MOA-B and PDE-4 (Frutarom internal data). On basis of these data, we suggest widening the extraction solvent range to 15-50% ethanol. - In addition, dry extracts should be added in order to cover existing preparations currently on the market. - The expressed juice from the fresh herb is marketed in Germany as “Schoenenberger naturreiner Heilpflanzensaft Hafer” since more than 30 years. <p><u>Note:</u> The internal Frutarom data mentioned in our comment on section 2. can be provided by the company upon request of the HMPC.</p>	<ul style="list-style-type: none"> - Endorsed. - The % ethanol can be widened if the data referred to can be submitted in order to complete the assessment report. - Endorsed. - Endorsed.
<p>3. PHARMACEUTICAL FORM</p> <p>Herbal substance or herbal preparations in solid or liquid dosage forms for oral use or as herbal tea.</p>	<p>We refer to our comments above.</p>	<p>... <i>for oral use</i> ... will be sufficient</p>

<p>4.2 Posology and method of administration</p> <p>Posology</p> <p><i>Adolescents over 12 years of age, adults, elderly</i></p> <p>Single dose Comminuted Cut or powdered herbal substance: 3 g</p> <p>Liquid extracts (1:5; ethanol 45 % v/v): 0.2 to 5 ml up to 3 times daily</p> <p>Expressed juice from the fresh herb: 3-4 times daily 10 ml.</p> <p>Other preparations corresponding to the daily dose of 3 g dried herbs.</p> <p>The use is not recommended in children under 12 years of age (see section 4.4 Special warnings and precautions for use).</p> <p>Duration of use</p> <p>Not to be taken for more than 2 weeks. No restrictions.</p> <p>If the symptoms persist during the use of the medicinal product medical advice should be sought.</p> <p>Method of administration</p> <p>Oral use.</p>	<p>We suggest changing the daily dose for all herbal preparations to the equivalent of the daily dose of herbal substance. The dosage recommendation for the expressed juice from the fresh herb is in accordance with the preparation “Schoenenberger naturreiner Heilpflanzensaft Hafer”.</p> <p>There is no evidence justifying a duration of use of maximum 2 weeks. On the contrary, the Commission E monograph mentions the treatment of chronic anxiety and stress with <i>Avena sativa</i>.</p>	<p>- Not endorsed. ‘Comminuted’ is the common term used in other monographs. It is preferable to keep this wording in the monograph.</p> <p>- Endorsed. Monograph amended in line with other herbal sedatives.</p> <p>- The dose of the expressed fruit juice is accepted.</p> <p>- Dose expression as an equivalent of the herb is acceptable.</p>
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<p>4.4 Special warnings and precautions for use</p> <p><u>Traditional use</u></p> <p>The use is not recommended in children under 12 years of age due to the lack of adequate data.</p> <p>Caution is advised when used in patients with coeliac disease because data on the protein content are missing.</p> <p>For liquid extracts containing ethanol, the appropriate labelling for ethanol, taken from the ‘Guideline on excipients in the label and packaging leaflet of medicinal products for human use’, must be included.</p>	<p>Data from clinical studies show that no effects were observed on coeliac patients on an oat rich diet for 5 years (Janatuinen et al 2002 – reference enclosed).</p>	<p>Not endorsed.</p> <p>Janatuinen et al. is already enclosed in the list of references. This study has a relative value: - after 5 years only 23 patients of 45 were still on an oats diet;</p> <ul style="list-style-type: none"> - the frequency of immunoreactivity was comparable in the intervention versus the control group: abnormal values of antibodies were attributed to non compliance with the gluten free diet; - the study was done with a specific preparation not comparable with <i>Avena herba</i>. <p>The formulation can be kept in the monograph: it has the character of a warning when the protein content is not known.</p>
<p>4.4. Special warnings and precautions for use</p>	<p>As the herb harvested before the flowering period expresses no grains, a precaution for patients with coeliac disease seems not to be substantiated and should be deleted.</p>	<p>Not endorsed..</p> <p>See comments above.</p>
<p>4.5 Interactions with other medicinal products and other forms of interaction</p> <p>Concomitant use with synthetic sedatives is not recommended unless advised by a doctor.</p> <p>None reported.</p>	<p>There is no evidence of any existing drug interactions with <i>Avena sativa</i>. We therefore object to this statement</p>	<p>Endorsed. Monograph amended in line with other herbal sedatives.</p>

<p>4.5. Interactions with other medicinal products and other forms of interaction</p>	<p>As neither data on such interactions nor data on sedative actions and effects are available, the warning not to use concomitantly with synthetic sedatives seems not to be substantiated and should be deleted.</p>	<p>Endorsed. See comment above.</p>
<p>4.7 Effects on ability to drive and use machines</p> <p>No studies on the effect in the ability to drive and use machines have been performed.</p> <p>May impair ability to drive and use machines Affected patients should not drive or operate machinery.</p>	<p>As neither data on such interactions nor data on sedative actions and effects are available, the warning not to use concomitantly with synthetic sedatives seems not to be substantiated and should be deleted.</p>	<p>Warning brought in line with other herbal sedative monographs.</p> <p>May impair ability to drive and use machines Affected patients should not drive or operate machinery.</p>
<p>4.7 Effects on ability to drive and use machines</p>	<p>As no studies investigated the effect on the ability to drive and use machines and data on sedative actions are not available, the warning of “May impair ability to drive and use machines” is not substantiated and should be deleted.</p>	<p>See comment above.</p>
<p>Comment on the list of references</p>	<p>The pharmaceutical quality of the herb (harvested before flowering season) or fruits is different and different data are relevant for each of both drugs; by combining the data for both drugs in one list of references, such detailed information is not more available for any assessment. Therefore, there should be a separate list of references for each of both monographs.</p>	<p>Not endorsed. The list of references is clear when read in conjunction with the Assessment Report.</p>