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**COMMITTEE ON HERBAL MEDICINAL PRODUCTS
(HMPC)**

DRAFT

COMMUNITY HERBAL MONOGRAPH ON *PIMPINELLA ANISUM L.*, FRUCTUS

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DRAFT COMMUNITY HERBAL MONOGRAPH ON *PIMPINELLA ANISUM L.*, FRUCTUS

1. NAME OF THE MEDICINAL PRODUCT

To be specified for the individual finished products.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION¹

<u>Well-established use</u>	<u>Traditional use</u>
With regard to the marketing authorisation application of Article 10(a) of Directive 2001/83/EC as amended	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended <i>Pimpinella anisum</i> L., fructus (Aniseed) i) Herbal substance: dried aniseed ii) Herbal preparation a) Aniseed, comminuted

3. PHARMACEUTICAL FORM

<u>Well-established use</u>	<u>Traditional use</u>
	Herbal substance or herbal preparation in solid or liquid dosage forms for oral use (to be described according to the standard terms published by the European Pharmacopoeia).

¹ The material complies with the Ph. Eur. The declaration of all active substances should be as expressed in the Guideline on the Quality of herbal medicinal products/traditional herbal medicinal products, CPMP/QWP/2819/00 Rev 1 and EMEA/CVMP/814/00 Rev 1. and if relevant, type of extracts should be specified as defined in the general monograph on Extracts of the Ph. Eur. (ref 765).

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

<u>Well-established use</u>	<u>Traditional use</u>
None	<p>i) Traditional herbal medicinal product for symptomatic treatment of mild, spasmodic gastro-intestinal complaints including bloating and flatulence.</p> <p>ii) Traditional herbal medicinal product used as an expectorant in cough and cold.</p> <p>The product is a traditional herbal medicinal product for use in specified indications exclusively based on long standing use.</p>

4.2. Posology and method of administration

<u>Well-established use</u>	<u>Traditional use</u>
	<p><i>Adults:</i></p> <p>Indication i): 3,5 g of (freshly²) comminuted aniseed as a herbal tea.</p> <p>Indication ii): a single dose 2-3 times daily. A single dose consists of 1-5 g of crushed fruits in 150 ml of water as a herbal tea.</p> <p>The use in children is not recommended due to the lack of adequate data for safety assessment.</p> <p>Duration of administration Not to be taken for more than two weeks.</p> <p>Method of administration Oral use.</p> <p>If the symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.</p>

² For commercial preparations of crushed aniseed the applicant must carry out appropriate stability testing related to the content of essential oil components

4.3. Contraindications

<u>Well-established use</u>	<u>Traditional use</u> Patients with known sensitivity to Apiaceae (Umbelliferae) (fennel, caraway, coriander and dill) or to anethol.
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4.4. Special warnings and precautions for use

<u>Well-established use</u>	<u>Traditional use</u> Patients with known sensitivity to Asteraceae (Compositae) should avoid the use of aniseed, because of cross-reactivity risk.
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4.5. Interaction with other medicinal products and other forms of interaction

<u>Well-established use</u>	<u>Traditional use</u> Not known
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4.6. Pregnancy and lactation

<u>Well-established use</u>	<u>Traditional use</u> There are no data from the use of aniseed in pregnant patients. Studies in animals have shown reproductive toxicity of trans-anethol (the major constituent of anise oil) (see section 5.3) It is unknown if aniseed constituents are excreted in human breast milk. In absence of sufficient data the use during pregnancy and lactation is not recommended.
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4.7. Effects on ability to drive and use machines

<u>Well-established use</u>	<u>Traditional use</u> No studies on the effect on the ability to drive and use machines have been performed.
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4.8. Undesirable effects

<u>Well-established use</u>	<u>Traditional use</u>
	<p>Allergic reactions affecting the skin, the respiratory and gastro-intestinal system may occur.</p> <p>If other adverse reactions not mentioned above occur a doctor or a qualified health care practitioner should be consulted.</p>

4.9. Overdose

<u>Well-established use</u>	<u>Traditional use</u>
	No case of overdose has been reported

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

<u>Well-established use</u>	<u>Traditional use</u>
	<p>Not required as per Article 16c(1)(a) iii) of Directive 2001/83/EC as amended</p> <p>The traditional medicinal use of aniseed has been largely due to antispasmodic, secretolytic, expectorant and antibacterial effects of its essential oil.</p> <p>Secretolytic and expectorant effects may be due to the content of anethol in the plant. Aqueous extract may exert bronchodilatory effect.</p> <p>Aniseed extracts exhibit <i>in vitro</i> inhibitory activities against the growth of a wide spectrum of bacteria and fungi known to be pathogenic for man and other species.</p>

5.2. Pharmacokinetic properties

<u>Well-established use</u>	<u>Traditional use</u>
	<p>Not required as per Article 16c(1)(a) iii) of Directive 2001/83/EC as amended</p> <p>No data available for aniseed in human beings or animals.</p> <p>After oral administration the compound trans-anethol is rapidly absorbed. 54-69% of the dose is eliminated in the urine and 13-17% in exhaled carbon dioxide. Trans-anethol is reported to be metabolized by O-demethylation and by oxidative transformation of the C3-side chain. The bulk of elimination occurred within 8 hours. The principal metabolite is 4-methoxyhippuric acid.</p>

5.3. Preclinical safety data

<u>Well-established use</u>	<u>Traditional use</u>
	<p>Not required as per Article 16c(1)(a) iii) of Directive 2001/83/EC as amended, unless necessary for the safe use of the product.</p> <p>For trans-anethol at high doses (50, 70, 80 mg/kg body weight) dose-dependent anti-implantation, early abortifacient and antifertility activity has been reported in rats.</p> <p>Trans-anethol is reported as “generally recognized as safe” (GRAS) at the intake of 54 µg/kg body weight/day)</p> <p>The acceptable daily intake (ADI) established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) is 0-2 mg/kg body weight.</p> <p>An extract prepared with water was tested in an Ames test on <i>Salmonella typhimurium</i> strains TA98, TA100, TA102 and turned out as negative. Results from studies carried out in the laboratory animals showed a weak mutagenic potential of anethol.</p> <p>The genotoxic risk related to estragole (EMEA/HMPC/137212/2005) is not considered to be relevant due to the small amount present in herbal infusions prepared from aniseed.</p>

6. PHARMACEUTICAL PARTICULARS

<u>Well-established use</u>	<u>Traditional use</u>
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7. DATE OF COMPILATION/LAST REVISION

7 September 2006