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

FINAL

**COMMUNITY HERBAL MONOGRAPH ON
*LINUM USITATISSIMUM L., SEMEN***

DISCUSSION IN THE DRAFTING GROUP ON SAFETY & EFFICACY	May 2005 June 2005 September 2005
ADOPTION BY HMPC FOR RELEASE FOR CONSULTATION	20 September 2005
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KEYWORDS	Herbal medicinal products; HMPC; Community herbal monograph; well-established use; traditional use; linseed; <i>Linum usitatissimum L.</i>
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COMMUNITY HERBAL MONOGRAPH ON
LINUM USITATISSIMUM L., SEMEN

1. NAME OF THE MEDICINAL PRODUCT

To be specified for the individual finished product.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION^{1,2}

<u>Well-established use</u>	<u>Traditional use</u>
<p>With regard to the marketing authorisation application of Article 10a of Directive 2001/83/EC as amended</p> <p><i>Linum usitatissimum L., semen (linseed)</i></p> <ul style="list-style-type: none"> • Herbal substance - dried, ripe seeds • Herbal preparation <i>not covered</i> 	<p>With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended</p> <p><i>Linum usitatissimum L., semen (linseed)</i></p> <ul style="list-style-type: none"> • Herbal substance - dried, ripe seeds (for use as a mucilaginous preparation only) • Herbal preparations - mucilaginous preparations of the dried ripe seeds

3. PHARMACEUTICAL FORM

<u>Well-established use</u>	<u>Traditional use</u>
<p>Herbal substance for oral use. The pharmaceutical form should be described by the European Pharmacopeia full standard term.</p>	<p>Mucilaginous preparation of the herbal substance for oral use. The pharmaceutical form should be described by the European Pharmacopeia full standard term.</p>

¹ The material complies with the Ph. Eur. monograph.

² The declaration of the active substance(s) should be in accordance with relevant herbal quality guidance.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

<u>Well-established use</u>	<u>Traditional use</u>
Herbal medicinal product for the treatment of habitual constipation or in conditions in which easy defaecation with soft stool is desirable.	Traditional herbal medicinal product for use as a demulcent preparation for the symptomatic relief of mild gastrointestinal discomfort. The product is a traditional herbal medicinal product for use in specified indication(s) exclusively based upon long-standing use.

4.2. Posology and method of administration

<u>Well-established use</u>	<u>Traditional use</u>
Posology Oral use Daily dose <i>Adolescents over 12 years of age, adults, elderly</i> 10 - 15 g, 2 - 3 times daily Method of administration Take 10 - 15 g seeds with 150 ml water, milk, fruit juice or similar aqueous liquid 2 - 3 times daily; then maintain adequate fluid intake. The product should be taken during the day at least ½ to 1 hour before or after intake of other medicines. The effect starts 12 - 24 hours later. Warning: not to be taken immediately prior to bedtime. Duration of use If the constipation does not resolve within 3 days, a doctor or a pharmacist should be consulted. See also section 4.4 Special warnings and precautions for use	Posology Oral use Single dose <i>Adolescents over 12 years of age, adults, elderly</i> For a mucilaginous preparation, soak 5 - 10 g whole or broken seeds in 250 ml water and take this half an hour before eating up to three times during the day. If possible soak the seeds the evening before. The mucilaginous preparations may be consumed with or without the seeds. <i>A minimal definite period can be given in which the seeds have to be soaked. If it is proven for the specific preparation that the seeds do not swell more, the wordings concerning bulk formers (i.e. contraindications, special warnings, interactions, undesirable effects) can be omitted.</i> Duration of use If the symptoms persist for more than 1 week during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

4.3. Contraindications

<u>Well-established use</u>	<u>Traditional use</u>
Linseed should not be used by patients with a sudden change in bowel habit that persists for more than 2 weeks, undiagnosed rectal bleeding and failure to defaecate following the use of a laxative. Linseed should also not be used by patients suffering from abnormal constrictions in the gastro-intestinal tract, with diseases of the oesophagus and cardia or existing intestinal blockage (ileus), paralysis of the intestine or megacolon.	Linseed should not be used by patients with melanorrhoea, potential or existing intestinal blockage (ileus), paralysis of the intestine or megacolon or by patients with a sudden change in bowel habit that persists for more than 2 weeks. Linseed should also not be used by patients suffering from abnormal constrictions in the gastro-intestinal tract, with diseases of the oesophagus and cardia.

<p>This product should not be taken by patients, who have difficulty swallowing or any throat problems.</p> <p>Patients with known hypersensitivity to the active substance should not use linseed.</p>	<p>This product should not be taken by patients, who have difficulty swallowing or any throat problems.</p> <p>Patients with known hypersensitivity to the active substance should not use linseed and its preparations.</p>
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4.4. Special warnings and precautions for use

<u>Well-established use</u>	<u>Traditional use</u>
<p>Because there is insufficient experience available, use is not recommended in children below the age of 12 years.</p> <p>If abdominal pain occurs or in cases of any irregularity of faeces, the use of linseed should be discontinued and medical advice must be sought.</p> <p>Linseed should not be used by patients with faecal impaction and symptoms such as abdominal pain, nausea and vomiting unless advised by a doctor because these symptoms can be signs of potential or existing intestinal blockage (ileus.)</p> <p>In the package leaflet, the patient is informed about the following warning:</p> <p>Warnings Take each single dose of this product with at least 150 ml of water or similar aqueous fluid. Taking this product without adequate fluid, may cause it to swell and block your throat or oesophagus and may cause choking. Intestinal obstruction may occur if adequate fluid intake is not maintained. If you experience chest pain, vomiting, or difficulty in swallowing or breathing after taking this product, seek immediately medical attention. The treatment of debilitated patients and elderly should be supervised.</p> <p>Investigations in healthy women suggest that linseed may have an oestrogenic effect, use is therefore not recommended in women with hormonally dependent tumours.</p>	<p>Because there is insufficient experience available, use of this product is not recommended in children below the age of 12 years.</p> <p>Linseed should not be used by patients with faecal impaction and symptoms such as abdominal pain, nausea and vomiting unless advised by a doctor because these symptoms can be signs of potential or existing intestinal blockage (ileus.)</p> <p>In the package leaflet, the patient is informed about the following warning:</p> <p>Warnings Take each single dose of this product with at least 150 ml of water or similar aqueous fluid. Taking this product without adequate fluid, may block your throat or oesophagus and may cause choking. Intestinal obstruction may occur if adequate fluid intake is not maintained. If you experience chest pain, vomiting, or difficulty in swallowing or breathing after taking this product, seek immediately medical attention. The treatment of debilitated patients and elderly should be supervised.</p> <p>Investigations in healthy women suggest that linseed may have an oestrogenic effect, use is therefore not recommended in women with hormonally dependent tumours.</p>

4.5. Interaction with other medicinal products and other forms of interaction

<u>Well-established use</u>	<u>Traditional use</u>
<p>Enteral absorption of concomitantly administered medicines may be delayed by bulk forming laxatives such as linseed.</p> <p>For this reason the product should not be taken ½ to 1 hour before or after intake of other medicinal products.</p>	<p>Enteral absorption of concomitantly administered medicines may be delayed by a demulcent preparation of linseed.</p> <p>For this reason the product should not be taken ½ to 1 hour before or after intake of other medicinal products.</p>

In order to decrease the risk of gastrointestinal obstruction (ileus), linseed should only be used together with medicinal products known to inhibit peristaltic movement (e.g. opioids, loperamide) under medical supervision.	In order to decrease the risk of gastrointestinal obstruction (ileus), linseed should only be used together with medicinal products known to inhibit peristaltic movement (e.g. opioids, loperamide) under medical supervision.
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4.6. Pregnancy and lactation

<u>Well-established use</u>	<u>Traditional use</u>
There are no reports of any harmful or deleterious effects during pregnancy and lactation. Investigations in healthy women suggest that linseed may have an oestrogenic effect. As there are insufficient systematic data available, use is not recommended during pregnancy and lactation.	There are no reports of any harmful or deleterious effects during pregnancy and lactation. Investigations in healthy women suggest that linseed may have an oestrogenic effect. As there are insufficient systematic data available, use is not recommended during pregnancy and lactation.

4.7. Effects on ability to drive and use machines

<u>Well-established use</u>	<u>Traditional use</u>
Not relevant.	Not relevant.

4.8. Undesirable effects

<u>Well-established use</u>	<u>Traditional use</u>
Meteorism, occurring with the use of the product, is common. Reactions of hypersensitivity including anaphylaxis-like reactions may occur very rarely. If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.	Meteorism, occurring with the use of the product, is common. Reactions of hypersensitivity including anaphylaxis-like reactions may occur very rarely. If other adverse reactions not mentioned above occur, a doctor or a qualified health care practitioner should be consulted.

4.9. Overdose

<u>Well-established use</u>	<u>Traditional use</u>
Overdose with linseed may cause abdominal discomfort, flatulence and possibly intestinal obstruction. Adequate fluid intake should be maintained and management should be symptomatic.	Overdose with linseed may cause abdominal discomfort, flatulence and possibly intestinal obstruction. Adequate fluid intake should be maintained and management should be symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

<u>Well-established use</u>	<u>Traditional use</u>
Pharmacotherapeutic group: Laxatives - Bulk Producers	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

<p>ATC-Code: A 06 AC</p> <p>The active ingredient linseed consists of the dried, ripe seeds of <i>Linum usitatissimum</i> L.</p> <p>The seeds contain nearly 25 % of bulk materials (3 - 6 % of mucilage, 4 - 7 % of alimentary fibres). The laxative effects of linseed have long been recognised empirically and shown in animal and clinical investigations. These effects are attributed to the bulk materials and in particular to the mucilage that binds with water and swells to form a demulcent gel in the intestine. Water is held back in the intestine due to the swelling of the mucilage. Faeces become softer. The volume of the intestinal content increases and causes a stretch stimulus, which results in a decrease in transit time. The swollen mass of mucilage forms a lubrication layer facilitating the transit of intestinal content.</p> <p><i>Progress of action:</i> Linseed usually acts within 12 to 24 hours. Sometimes the maximum effect is not reached before 2 or 3 days.</p> <p>Broken seeds do not always cause a stretch stimulus because the increase in volume may already start in the stomach. Whole or “bruised seeds” have a delayed increase in volume.</p> <p>The use as a laxative is made plausible by information from clinical studies and pharmacological data.</p> <p>The use in conditions, in which easy defaecation with soft stool is desirable, is scientifically substantiated on the basis of the laxative effects but there are no special data available.</p>	
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5.2. Pharmacokinetic properties

<p><u>Well-established use</u></p> <p>One part of the bulk materials in linseed is defaecated, the other part is fermented in the colon by bacteria. This process of fermentation can produce gas and flatulence. The predominant products of fermentation are short chain fatty acids (SCFA), which are mainly resorbed.</p>	<p><u>Traditional use</u></p> <p>Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.</p>
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5.3. Preclinical safety data

<p><u>Well-established use</u></p> <p>Linseed contains 20-50 mg cyanide/100 g in form of the cyanogenic diglycosides linustatin, neolinustatin and small amount of the</p>	<p><u>Traditional use</u></p> <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>
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<p>monoglucoside linamarin. Neither a single dosage of 100 g linseed nor a chronic dose of 45 - 50 g daily for 4 - 6 weeks cause intoxication signs in man.</p> <p>The enzyme thiosulphate sulphur transferase (rhodanase) catalyzes the change of cyanide into thiocyanate (rhodanide), which is 200 times less toxic than cyanide. The chronic use of linseed causes accumulation of thiocyanate, which can be compared with the blood level of thiocyanate in heavy smokers.</p> <p>Investigations in healthy women suggest that there might be an oestrogenic effect of linseed due to the lignan-precursors in linseed, which are converted to mammalian-lignans and might interfere with the metabolism and activity of oestrogens.</p> <p>Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.</p>	<p>Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.</p>
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6. PHARMACEUTICAL PARTICULARS

<u>Well-established use</u>	<u>Traditional use</u>
Inappropriate storage of linseed may lead to a higher content of cyanogenic glycosides.	Inappropriate storage of linseed may lead to a higher content of cyanogenic glycosides.

7. DATE OF COMPILATION/LAST REVISION

26 October 2006