European Medicines Agency
Evaluation of Medicines for Human Use

London, 26 October 2006
Doc. Ref. EMEA/HMPC/340857/2005

COMMITTEE ON HERBAL MEDICINAL PRODUCTS (HMPC)

FINAL

COMMUNITY HERBAL MONOGRAPH ON *PLANTAGO OVATA* FORSSK., SEMINIS TEGUMENTUM

DISCUSSION IN THE DRAFTING GROUP ON SAFETY & EFFICACY	May 2005 June 2005 September 2005
ADOPTION BY HMPC FOR RELEASE FOR CONSULTATION	20 September 2005
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 January 2006
REDISCUSSION IN WORKING PARTY ON COMMUNITY MONOGRAPHS AND COMMUNITY LIST	May 2006 July 2006
ADOPTION BY HMPC	13 July 2006

KEYWORDS	Herbal medicinal products; HMPC; Community herbal monograph; well-established use; ispaghula husk; *Plantago ovata* Forssk.

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COMMUNITY HERBAL MONOGRAPH ON
***PLANTAGO OVATA* FORSSK., SEMINIS TEGUMENTUM**

1. NAME OF THE MEDICINAL PRODUCT

To be specified for the individual finished product.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION [1, 2]

Well-established use	Traditional use
With regard to the marketing authorisation application of Article 10a of Directive 2001/83/EC as amended *Plantago ovata* Forssk. (*P. ispaghula* Roxb.), seminis tegumentum (ispaghula husk) • Herbal substance - episperm and collapsed adjacent layers removed from the seeds • Herbal preparation - powdered herbal substance	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended

3. PHARMACEUTICAL FORM

Well-established use	Traditional use
Herbal substance or herbal preparation in solid dosage forms such as granules or powders for oral use. The pharmaceutical form should be described by the European Pharmacopeia full standard term.	

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Well-established use	Traditional use
Herbal medicinal product a) for the treatment of habitual constipation; b) in conditions in which easy defaecation with	

[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.

soft stool is desirable, e.g. in cases of painful defaecation after rectal or anal surgery, anal fissures and haemorrhoids; c) in patients to whom an increased daily fibre intake may be advisable e.g. as an adjuvant in constipation predominant irritable bowel syndrome, as an adjuvant to diet in hypercholesterolemia (see section 4.4 Special warnings and precautions for use and section 5.1 Pharmacodynamic properties).	

4.2 Posology and method of administration

Well-established use	Traditional use
Posology Oral use Indications a) and b) *Adolescents over 12 years of age, adults, elderly* 7 - 11 g herbal substance or corresponding amount of herbal preparation (daily dose) in 1 - 3 single doses. *Children from 6 to 12 years of age* Half to two-thirds of the adult dose (3 - 8 g herbal substance or corresponding amount of herbal preparation, daily dose) in 1 - 3 single doses Indication c) *Adolescents over 12 years of age, adults, elderly* 7 - 20 g herbal substance or corresponding amount of herbal preparation (daily dose) in 1 - 3 single doses **Method of administration** Mix approximately x g of the [pharmaceutical form] (amount corresponding to 1 g herbal substance) with at least 30 ml of water, milk, fruit juice or similar aqueous liquid; stir briskly and swallow as quickly as possible. Alternatively the herbal substance can be taken and swallowed with sufficient quantity (at least 30 ml per g of herbal substance) of water, milk, fruit juice or similar aqueous liquid; 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 bed-time. **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.	

4.3 Contraindications

Well-established use	Traditional use
Ispaghula husk 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. Ispaghula husk should also not be used by patients suffering from abnormal constrictions in the gastro-intestinal tract, with diseases of the oesophagus and cardia, potential or existing intestinal blockage (ileus), paralysis of the intestine or megacolon, diabetes mellitus, which is difficult to regulate. This product should not be taken by patients who have difficulty in swallowing or any throat problems. Patients with known hypersensitivity to the active substance should not use ispaghula husk and its preparations.	

4.4 Special warnings and precautions for use

Well-established use	Traditional use
As there is insufficient experience available, - use is not recommended in children below the age of 6 years for indications a) and b). Laxative bulk producers should be used before using other purgatives if change of nutrition is not successful; - use is not recommended in children below the age of 12 years for indication c). Ispaghula husk 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). Indication a) If abdominal pain occurs or in cases of any irregularity of faeces, the use of ispaghula husk should be discontinued and medical advice must be sought. Indication c) The use of ispaghula husk as an adjuvant to diet in hypercholesterolemia requires medical supervision.	

A sufficient amount of liquid should always be taken e.g. 30 ml of water per 1 g of herbal substance. In the package leaflet, the patient is informed about the following warning: **Warning** Take each single dose of this product with at least x ml (x is to be replaced by the amount which corresponds to 30 ml per 1 g of the herbal substance or corresponding amount of the herbal preparation) 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 immediate medical attention. The treatment of debilitated patients requires medical supervision. The treatment of elderly patients should be supervised.	

4.5 Interaction with other medicinal products and other forms of interaction

Well-established use	Traditional use
Enteral absorption of concomitantly administered medicines such as minerals, vitamins (B 12), cardiac glycosides, coumarin derivatives, carbamazepine and lithium may be delayed. For this reason the product should not be taken ½ to 1 hour before or after intake of other medicinal products. If the product is taken together with meals by insulin dependent diabetic patients it may be necessary to reduce the insulin dose. Use of ispaghula husk concomitantly with thyroid hormones requires medical supervision because the dose of the thyroid hormones may have to be adjusted. In order to decrease the risk of gastrointestinal obstruction (ileus) ispaghula husk should be used together with medicinal products known to inhibit peristaltic movement (e.g. opioids, loperamide) only under medical supervision.	

4.6 Pregnancy and lactation

Well-established use	Traditional use
No restriction. Laxative bulk producers should be used before using other purgatives if change of nutrition is not successful.	

4.7 Effects on ability to drive and use machines

Well-established use	Traditional use
Not relevant.	

4.8 Undesirable effects

Well-established use	Traditional use
Flatulence may occur with the use of the product, this generally disappears in the course of the treatment. Abdominal distension and risk of intestinal or oesophageal obstruction and faecal impaction may occur, particularly if swallowed with insufficient fluid. Due to the allergic potential of ispaghula, patients must be aware of reactions of hypersensitivity including very rare anaphylaxis-like reactions. If other adverse reactions not mentioned above occur, a doctor or a pharmacist should be consulted.	

4.9 Overdose

Well-established use	Traditional use
Overdose with ispaghula husk may cause abdominal discomfort, flatulence and possibly intestinal obstruction. Adequate fluid intake should be maintained and management should be symptomatic.	

5. PHARMACOLOGICAL PROPERTIES[3]

5.1 Pharmacodynamic properties

Well-established use	Traditional use
Pharmacotherapeutic group: Laxatives – Bulk Producers, other Cholesterol and Triglyceride Reducers ATC-code: A 06 AC, C 10 AX The active ingredient ispaghula husk consists of the episperm and collapsed adjacent layers removed from the seeds of *Plantago ovata* Forssk (*Plantago ispaghula* Roxb.). Ispaghula husk is particularly rich in alimentary fibres and mucilages, its mucilage content being higher than that of other Plantago species. Ispaghula husk is capable of absorbing up to 40 times its own weight in water. Ispaghula husk consists of 85 % water-soluble fibre; it is partly fermentable (*in vitro* 72 % unfermentable residue) and acts by hydration in the bowel. Gut motility and transit rate can be modified by ispaghula husk through mechanical stimulation of the gut wall as a result of the increase in intestinal bulk by water and the decrease in viscosity of the luminal contents. When taken with a sufficient amount of liquid (at least 30 ml per 1 g of herbal substance) ispaghula husk produces an increased volume of intestinal contents due to its highly bulking properties and hence a stretch stimulus, which triggers defaecation; at the same time the swollen mass of mucilage forms a lubricating layer, which makes the transit of intestinal contents easier. *Progress of action*: Ispaghula husk usually acts as a laxative within 12 to 24 hours after single administration. Sometimes the maximum effect is reached after 2 to 3 days. In mild to moderate hypercholesterolemia a reduction of LDL cholesterol of approximately 7% has been reported. Investigations, which study the effect of ispaghula husk on the incidence of cardiovascular events and total mortality are not available.	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

[3] Scientific data available do not always differentiate the investigated preparations exactly whether the investigated herbal substance was ispaghula husk or seed or psyllium seed and often indicate "psyllium" as investigated herbal substance. If a differentiation was not possible the term "psyllium" is used.

5.2 Pharmacokinetic properties

Well-established use	Traditional use
The material hydrates and swells to form a mucilage because it is only partially solubilised. Polysaccharides, such as those which dietary fibres are made of, must be hydrolysed to monosaccharides before intestinal uptake can occur. The sugar residues of the xylan backbone and the side chains of psyllium are joined by ß-linkages, which cannot be broken by human digestive enzymes. Less than 10 % of the mucilage gets hydrolysed in the stomach, with formation of free arabinose. Intestinal absorption of the free arabinose is approximately 85 % to 93 %. To varying degrees, dietary fibre is fermented by bacteria in the colon, resulting in production of carbon dioxide, hydrogen, methane, water, and short-chain fatty acids, which are absorbed and brought into the hepatic circulation. In humans, psyllium reaches the large bowel in a highly polymerised form that is fermented to a limited extent, resulting in increased faecal concentration and excretion of short-chain fatty acids.	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

5.3 Preclinical safety data

Well-established use	Traditional use
Single dose toxicity The LD50 in rats was greater than the highest dose tested corresponding to 3,360 mg/kg ispaghula husk administered by gavage of an aqueous suspension. The LD50 in mice was greater than the highest dose tested corresponding to 2,940 mg/kg ispaghula husk also administered by gavage of an aqueous suspension. These studies were conducted prior to the establishment of good laboratory practices. **Subchronic toxicity** Psyllium was fed to rats at levels high as 10 % of the diet for periods up to 13 weeks (three 28-day studies, one 13-week study). Psyllium consumption ranged from 3,876 to 11,809 mg/kg/day. Because the absorption of psyllium is very limited, histopathological evaluations were limited to the gastrointestinal tract, liver, kidneys and gross lesions without observing any treatment-related effect. Effects considered to be biologically significant and related to psyllium supplementation were lower serum total protein, albumin, globulin, total iron-binding capacity, calcium, potassium, and	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.

cholesterol; and higher aspartate transaminase (AST) and alanine transaminase (ALT) activities relative to control. Several of these effects are considered to be secondary effects to others. The reasons for the lower serum total protein, albumin and globulin are not clear, but the absence of any increases in urinary protein, any evidence of gastrointestinal pathology, which could account for protein loss, and any differences in growth or feed efficiency in psyllium fed rats may give evidence that there are no adverse effect of psyllium on protein metabolism. **Reproductive toxicity** A rat multigeneration reproduction/teratology study showed no evidence of any adverse effects of psyllium on reproduction or development. Psyllium as 0, 1.25, or 5% (w/w) of the diet was administered in a standard (NIH-07) rat and mouse meal diet *ad libitum* through gestation of the third generation. A segment II study in rabbits also showed no evidence of any adverse effect. Psyllium as 0, 2.5, 5 or 10% (w/w) of diet was administered in a purine certified rabbit chow diet for days 2 - 20 of gestation. **Genotoxicity and carcinogenicity** Tests on genotoxicity and carcinogenicity have not been performed.	

6. PHARMACEUTICAL PARTICULARS

Well-established use	Traditional use
Not applicable.	

7. DATE OF COMPILATION/LAST REVISION

26 October 2006