EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

14 May 2013
EMA/HMPC/199774/2012
Committee on Herbal Medicinal Products (HMPC)

Community herbal monograph on *Plantago ovata* Forssk., seminis tegumentum

Final

Initial assessment	
Discussion in Working Party on Community monographs and Community list (MLWP)	May 2005 June 2005 September 2005
Adoption by Committee on Herbal Medicinal Products (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 (MLWP)	May 2006 July 2006
Adoption by Committee on Herbal Medicinal Products (HMPC) Monograph (EMEA/HMPC/340857/2005) AR (EMEA/HMPC/165838/2006) List of references (EMEA/HMPC/165832/2006) Overview of comments received during the public consultation (EMEA/HMPC/65916/2006) HMPC Opinion (EMEA/HMPC/353208/2006)	13 July 2006
First systematic review	
Discussion in Working Party on Community monographs and Community list (MLWP)	March 2012 May 2012 September 2012 November 2012 March 2013
Adoption by Committee on Herbal Medicinal Products (HMPC) for release for consultation	N/A
End of consultation (deadline for comments)	N/A
Rediscussion in Working Party on Community monographs and Community list (MLWP)	N/A
Adoption by Committee on Herbal Medicinal Products (HMPC)	14 May 2013

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7051
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

A search for the versions adopted in July 2006 can be made via the EMA document search function, using the documents' reference number, at:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/document_library_search.jsp&mid=

Keywords	Herbal medicinal products; HMPC; Community herbal monographs; well-established medicinal use; ispaghula husk; *Plantago ovata* Forssk., seminis tegumentum, Plantaginis ovatae seminis tegumentum

BG (bălgarski): Яйцевиден живовлек, семенна обвивка CS (čeština): osemení jitrocele vejčitého DA (dansk): Loppefrøskaller DE (Deutsch): Indische Flohsamenschalen EL (elliniká): ισπαγούλης φλοιός σπερμάτων EN (English): Ispaghula Husk ES (espanol): Ispágula, cutícula seminal de ET (eesti keel): kõrbe-teelehe seemnekest FI (suomi): ispagula, siemenkuori FR (français): Ispaghul (tégument de la graine d') HU (magyar): Egyiptomi útifű maghéj IT (italiano): Ispagula tegumento	LT (lietuvių kalba): Kiaušininių gysločių sėklų luobelės LV (latviešu valoda): Olveida ceļtekas sēklapvalki MT (malti): Qoxra taż-Żerriegħa tal-brigħed NL (nederlands): Psylliumzemel PL (polski): Łupina nasienna babki jajowatej PT (português): Ispagula, tegumento da semente RO (română): SK (slovenčina): Osemenie skorocelu vajcovitého SL (slovenščina): semenska lupina jajčastega trpotca SV (svenska): Ispagulafröskal *IS (íslenska)*: *NO (norsk):* Ispaghulafrøskall

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 10(a) of Directive 2001/83/EC as amended *Plantago ovata* Forssk. (*P. ispaghula* Roxb.), seminis tegumentum (ispaghula husk) i) Herbal substance Episperm and collapsed adjacent layers removed from the seeds ii) Herbal preparations Powdered herbal substance	

3. Pharmaceutical form

Well-established use	**Traditional use**
Herbal substance for oral use; herbal preparation in solid dosage forms for oral use. The pharmaceutical form should be described by the European Pharmacopoeia full standard term.	

4. Clinical particulars

4.1. Therapeutic indications

Well-established use	**Traditional use**
Indication 1) Herbal medicinal product for the treatment of habitual constipation. Indication 2) Herbal medicinal product in conditions in which	

[1] The material complies with the Eur. Ph. monograph (ref.: 01/2008:1334).
[2] The declaration of the active substance(s) for an individual finished product should be in accordance with relevant herbal quality guidance.

Well-established use	**Traditional use**
easy defaecation with soft stool is desirable, e.g. in cases of painful defaecation after rectal or anal surgery, anal fissures and haemorrhoids. Indication 3) Herbal medicinal product 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 Indication 1) and 2) *Adolescents, adults and elderly* Daily dose 7 – 11 g herbal substance/herbal preparation in 1 – 3 single doses *Children from 6 to 12 years of age* Daily dose 3 – 8 g herbal substance/herbal preparation in 1 – 3 single doses. The use in children under 6 years of age is not recommended (see section 4.4 'Special warnings and precautions for use'). Indication 3) *Adolescents, adults and elderly* Daily dose 7 – 20 g herbal substance/herbal preparation in 1 – 3 single doses The use in children under 12 years of age is not recommended (see section 4.4 'Special warnings and precautions for use'). **Duration of use** Indication 1) If the symptoms persist during the use of the medicinal product longer than 3 days, a doctor or a pharmacist should be consulted (see section 4.4	

Well-established use	Traditional use
'Special warnings and precautions for use'). **Method of administration** A sufficient amount of liquid (water, milk, fruit juice or similar aqueous liquid) should always be taken e.g. 30 ml of water per 1 g of herbal substance. The medicinal product can be mixed with the liquids and then swallowed or taken and then swallowed with sufficient quantity of liquid. Adequate fluid intake has to be maintained. The product should be taken during the day at least ½ to 1 hour before or after intake of other medicines, not immediately prior to bed-time. The effect starts 12 - 24 hours later. Powder formulations: When preparing the product for administration, it is important to try to avoid inhaling any of the powder in order to minimise the risk of sensitisation to the active ingredient.	

4.3. Contraindications

Well-established use	Traditional use
Hypersensitivity to the active substance (for powder formulations add: See section 4.4 'Special warnings and precautions for use'). Patients with a sudden change in bowel habit that persists for more than 2 weeks. Undiagnosed rectal bleeding and failure to defecate following the use of a laxative. 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. Patients who have difficulty in swallowing or any throat problems.	

4.4. Special warnings and precautions for use

Well-established use	Traditional use
Indication 1) and 2) The use is not recommended in children below 6 years of age due to insufficient data on efficacy. Laxative bulk producers should be used before using other purgatives if change of nutrition is not successful. Indication 3) The use is not recommended in children below 12 years of age due to insufficient data on efficacy. Indication 1), 2), 3) A sufficient amount of liquid should always be taken e.g. 30 ml of water per 1 g of herbal substance. 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). 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. When taken with inadequate fluid amounts, bulk forming agents can cause obstruction of the throat and oesophagus with choking and intestinal obstruction. Symptoms can be chest pain, vomiting, or difficulty in swallowing or breathing. The treatment of debilitated patients and / or elderly patients requires medical supervision. 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,) only under medical supervision. Powder formulations: <u>Warning on hypersensitive reactions</u> In individuals with continued occupational contact to powder of *Plantago ovata* seeds or husks (i.e. healthcare workers, caregivers) allergic	

Well-established use	Traditional use
sensitisation may occur due to inhalation, this is more frequent in atopic individuals. This sensitisation usually leads to hypersensitivity reactions which could be serious (see 4.8 'Undesirable effects'). It is recommended to assess clinically the possible sensitisation of individuals at risk and, if justified, to perform specific diagnostic tests. In case of proven sensitisation leading to hypersensitivity reactions, exposure to the product should be stopped immediately and avoided in the future (see 4.3 'Contraindications'). Indication 3) The use of ispaghula husk as an adjuvant to diet in hypercholesterolemia requires medical supervision.	

4.5. Interactions 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. Diabetic patients should take ispaghula husks only under medical supervision because adjustment of anti-diabetic therapy may be necessary. Use of ispaghula husk concomitantly with thyroid hormones requires medical supervision because the dose of the thyroid hormones may have to be adjusted.	

4.6. Fertility, pregnancy and lactation

Well-established use	Traditional use
There are limited amount of data (less than 300 pregnancy outcomes) from the use of ispaghula husk in pregnant women. Animal studies are insufficient with respect to reproductive toxicity	

Well-established use	Traditional use
(see section 5.3 'Preclinical safety data'). The use of ispaghula husk may be considered during pregnancy and lactation, if necessary and if change of nutrition is not successful. Laxative bulk producers should be used before using other purgatives. There is no evidence of an effect on the fertility in the rat following oral application (see section 5.3 'Preclinical safety data').	

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, which 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. The frequency is not known. Ispaghula contains potent allergens. The exposure to these allergens is possible through oral administration, contact with the skin and, in the case of powder formulations, also by inhalation. As a consequence to this allergic potential, individuals exposed to the product can develop hypersensitivity reactions such as rhinitis, conjunctivitis, bronchospasm and in some cases, anaphylaxis. Cutaneous symptoms such as exanthema and/or pruritus have also been reported. Special attention should be given to individuals manipulating the powder formulations routinely (see 4.4 'Special warnings and precautions for use'). The frequency is not known. 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 intestinal obstruction. Adequate fluid intake should be maintained and management should be symptomatic.	

5. Pharmacological properties

5.1. Pharmacodynamic properties

Well-established use	Traditional use
Pharmacotherapeutic group: {Laxatives – Bulk Producers, other Cholesterol and Triglyceride Reducers} Proposed ATC code: {A 06 AC 01, 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 defecation; 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.	

Well-established use	Traditional use
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.	

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 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, such fibre 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.	

5.3. Preclinical safety data

Well-established use	Traditional use
Ispaghula husk 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). The consumption ranged from 3,876 to 11,809 mg/kg/day (3-16 times of the human dosage calculated for a 60 kg human). Effects seen were lower serum total protein, albumin, globulin, total iron-binding capacity, calcium, potassium, and cholesterol; and higher aspartate	

Well-established use	Traditional use
transaminase and alanine transaminase activities relative to control. The absence of any increases in urinary protein and any differences in growth or feed efficiency in ispaghula husk fed rats may give evidence that there are no adverse effects on protein metabolism. Because the absorption of ispaghula husk is very limited, histopathological evaluations were limited to the gastrointestinal tract, liver, kidneys and gross lesions without observing any treatment-related effect. In a study on fertility, embryo-foetal development and pre- and postnatal development (multigeneration study) ispaghula husk (0, 1, 2.5, or 5% (w/w) of the diet) was administered continuously through two generations to rats. For fertility and foetal development and teratogenesis the NOAEL was 5% of the diet, while for offspring growth and development the NOAEL was given with 1% of the diet based on reductions in pup weights. The study on embryo-foetal development in rabbits (ispaghula husk as 0, 2.5, 5 or 10% (w/w) of diet) has to be considered as preliminary. Conclusions can not be drawn. 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

14 May 2013