EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee on Herbal Medicinal Products (HMPC)

Community herbal monograph on *Plantago afra* L. et *Plantago indica* L., semen

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/340865/2005) AR (EMEA/HMPC/167338/2006) List of references (EMEA/HMPC/244406/2006) Overview of comments received during the public consultation (EMEA/HMPC/65063/2006) HMPC Opinion (EMEA/HMPC/353137/2006)	13 July 2006
First systematic review	
Discussion in Working Party on Community monographs and Community list (MLWP)	September 2012 November 2012 March 2013
Adoption by Committee on Herbal Medicinal Products (HMPC) for release for consultation	N/A
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Rediscussion in Working Party on Community monographs and Community list (MLWP)	N/A
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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=

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Keywords	Herbal medicinal products; HMPC; Community herbal monographs; well-established medicinal use; psyllium seed; *Plantago afra* L., *Plantago indica* L., semen,

BG (bălgarski): Индийски живовлек, семе CS (čeština): chmelíkové semeno DA (dansk): Psylliumfrø DE (Deutsch): Flohsamen EL (elliniká): σπέρμα ψυλλίου EN (English): Psyllium Seed ES (espanol): Zaragatona, semilla de ET (eesti keel): teeleheseeme FI (suomi): rohtoratamo, siemen FR (français): Psyllium (graine de) HU (magyar): Nyálkás és homoki útifű mag IT (italiano): Psillio seme	LT (lietuvių kalba): Smiltyninių gysločių sėklos LV (latviešu valoda): Smilts ceļtekas sēklas MT (malti): Żerriegħa tal-Psilljum NL (nederlands): Vlozaad PL (polski): Nasienie płesznika PT (português): Psílio, semente RO (română): SK (slovenčina): Blškové semeno SL (slovenščina): seme indijskega trpotca SV (svenska): Loppfrö *IS (íslenska)*: *NO (norsk):* Loppefrø

Community herbal monograph on *Plantago afra* L. et *Plantago indica* L., semen

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 afra* L. (*Plantago psyllium* L.) or *Plantago indica* L. (*Plantago arenaria* Waldstein and Kitaibel), semen (psyllium seed) i) Herbal substance Ripe, whole, dry 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 monograph (ref.: 01/2008:0858).
[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 defecation with soft stool is desirable, e.g. in cases of painful defecation after rectal or anal surgery, anal fissures and haemorrhoids.	

4.2. Posology and method of administration

Well-established use	Traditional use
Posology *Adolescents, adults and elderly* Daily dose 25 - 40 g herbal substance/herbal preparation in 3 single doses *Children from 6 to 12 years of age* Daily dose 12 - 25 g herbal substance/herbal preparation in 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'). **Duration of use** If the constipation does not resolve within 3 days, a doctor or a pharmacist should be consulted. See section 4.4 '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.	

Well-established use	Traditional use
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
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. A sufficient amount of liquid should always be taken e.g. 30 ml of water per 1 g of herbal substance. Psyllium seed 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).	

Well-established use	Traditional use
If abdominal pain occurs or in cases of any irregularity of faeces, the use of psyllium seed 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) psyllium seed should be used together with medicinal products known to inhibit peristaltic movement (e.g. opioids) only under medical supervision. Powder formulations: Warning on hypersensitive reactions In individuals with continued occupational contact to powder of psyllium seeds (i.e. healthcare workers, caregivers) allergic 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').	

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	

Well-established use	Traditional use
1 hour before or after intake of other medicinal products. Diabetic patients should take psyllium seeds only under medical supervision because adjustment of anti-diabetic therapy may be necessary. Use of psyllium seed 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 no data from the use of psyllium seed, but limited data (less than 300 pregnancy outcomes) from the use of ispaghula husk in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3 Preclinical safety data). The use of psyllium seed 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. No fertility data available.	

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, with 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. Psyllium seed contains potent allergens. The exposure to these allergens is possible through	

Well-established use	Traditional use
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 psyllium seed 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} Proposed ATC code: {A 06 AC 01} The active ingredient psyllium seed consists of the dried ripe, whole seeds of Plantago afra L. (Plantago psyllium L.) or Plantago indica L. (Plantago arenaria Waldstein and Kitaibel). Psyllium seed is particularly rich in alimentary fibres and mucilages. Psyllium seed is capable of absorbing up to 10 times its own weight in water. Psyllium seed consists of 10 – 12 % mucilage polysaccharides, which are located in the episperms. It is partly fermentable (in vitro 72 % unfermentable residue) and acts by hydration in	

Well-established use	Traditional use
the bowel. Gut motility and transit rate can be modified by psyllium 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 or by contact with rough fibre particles. When taken with a sufficient amount of liquid (at least 30 ml per 1 g of herbal substance) psyllium 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*: Psyllium seed usually acts within 12 to 24 hours after single administration. Sometimes the maximum effect is reached after 2 to 3 days.	

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
No data are available for psyllium seed. Therefore data for ispaghula husk are mentioned. 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 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