SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Fybogel Mebeverine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

A sachet contains 3.5g ispaghula husk EP and 135mg mebeverine hydrochloride BP.

Excipients with known effect:
Each sachet contains aspartame (E951) 16 mg, sodium 58.65 mg and potassium 97.6 mg.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Granules for oral suspension in unit dose sachet

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic relief of irritable bowel syndrome

4.2 Posology and method of administration

The doctor should be consulted if you develop new symptoms, or if your symptoms worsen, or if symptoms do not improve after two weeks treatment (see section 4.4).

Posology

Adults and children over 12: One sachet morning and evening, taken half an hour before meals. A third dose may be taken before the midday meal if necessary.

Elderly: There is no indication that the dose need be modified for the elderly.

Children below 12: Not recommended (see section 4.4).

Method of Administration

The product is intended for oral administration as a suspension in water

(See section 4.4)

The contents of one sachet should be stirred into a glass of cold water (150 ml minimum) and drunk immediately.

The product should be taken during the day at least ½ to 1 hour before or after intake of other medicines and should not be taken immediately before going to sleep.

Effects may take 12-24 hours.

When preparing the product for administration, it is important to try to avoid inhaling any of the powder in order to minimize the risk of sensitisation to the active ingredient.

4.3 Contraindications

Hypersensitivity to ispaghula husk, mebeverine or to any of the excipients listed in section 6.1. (See Section 4.4).

Patients with a sudden change in bowel habit that has persisted more than two 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

The use is not recommended in children below 12 years of age due to insufficiency data on efficacy.

Laxative bulk producers should be used before using other purgatives if change of nutrition is not successful.

Fybogel Mebeverine should not be taken in the dry form and should always be taken mixed with fluid (5 fluid ounces or 150 mL of water or other liquid per sachet).

Gastrointestinal obstruction or impaction have been reported with hydrophilic mucilloid preparations when taken with insufficient liquid, contrary to administration instructions.

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 not be used together with medicinal products known to inhibit peristaltic movement (e.g. opioids) and then only under medical supervision (see section 4.5).

This product should not be taken immediately before going to bed as reduced gastric motility may impair intestinal passage and cause obstruction.

This medicine contains 16 mg aspartame in each unit dose (sachet). Aspartame is a source of phenylalanine. It may be harmful if you have phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

Consult your doctor if you have developed new symptoms, or if your symptoms worsen, or if they do not improve after two weeks of treatment.

Warning on hypersensitivity reactions: In individuals with continued occupational contact to powder of Plantago ovata seeds (e.g. healthcare workers and 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).

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).

This medicine contains 2.5 mmol (or 97.6 mg) potassium per sachet. To be taken into consideration by patients with reduced kidney function or patients on a controlled potassium diet.

The medicinal product contains 2.56 mmol (or 58.9 65mg) sodium per sachet, equivalent to 2.9% of the WHO recommended maximum daily intake of 2g sodium for an adult. To be taken into consideration by patients on a controlled sodium diet.

Mebeverine should be used with care in patients with hepatic or renal impairment, and those with cardiac disorders such as heart block.

4.5 Interaction with other medicinal products and other forms of interaction

Enteral absorption of concomitantly administered medicines such as minerals (such as calcium, iron, or zinc), vitamins (B12), 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 husk 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.

In order to decrease the risk of gastrointestinal obstruction, ispaghula husk should only be used together with medicinal products known to inhibit peristaltic movement (e.g. opioids, opioid-like agents and loperamide) if under medical supervision.

4.6 Fertility, pregnancy and lactation

Pregnancy

This product should be avoided during pregnancy.

There are limited data (less than 300 pregnancy outcomes) from the use of ispaghula husk in pregnant women. There are no or limited amounts of data from the use of mebeverine in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3a).

Breast-feeding

This product should not be used in breast-feeding.

Mebeverine or metabolites have been identified in breastfed newborns/infants of treated women. There is insufficient information on the effects of Mebeverine in newborns/infants.

Fertility

There are no clinical data on male or female fertility.

4.7 Effects on Ability to Drive and Use Machines

None known

4.8 Undesirable effects

The list of the following adverse effects relates to those experienced with ispaghula husk and mebeverine hydrochloride at OTC doses, in short term use.

In the treatment of chronic conditions, under long-term treatment, additional adverse effects may occur.
Special attention should be given to individuals manipulating the powder formulations routinely (see section 4.4). The frequency is not known.
Adverse events which have been associated with ispaghula husk or mebeverine are given below, tabulated by system organ class and frequency. Frequencies are defined as: Very common (≥1/10); Common (≥1/100 and <1/10); Uncommon (≥1/1000 and <1/100); Rare (≥1/10,000 and <1/1000); Very rare (< 1/10,000); Not known (cannot be estimated from the available data). Within each frequency grouping, adverse events are presented in order of decreasing seriousness.

System Organ Class	**Frequency**	**Adverse Events**
Immune System Disorders	Not Known	Hypersensitivity disorders[1, 2]
Eye Disorders	Not Known	Conjunctivitis[2]
Respiratory, Thoracic and Mediastinal Disorders	Not Known	Rhinitis[2]
Gastrointestinal Disorders	Not Known	Flatulence, abdominal distension, intestinal obstruction, oesophageal obstruction, faecal impaction[3]
Skin and Subcutaneous Tissue Disorders	Not Known	Skin Rash[2]

Description of Selected Adverse Reactions

1 Including rash, urticaria, anaphylactic reaction, pruritus, bronchospasm, rhinitis and angioedema.

2 Ispaghula/psyllium husk 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.

3 Flatulence and abdominal distension (bloating) may be experienced during the first few days of treatment, but should diminish during continued treatment. Abdominal distension and risk of intestinal or oesophageal obstruction and faecal impaction may occur, particularly if swallowed with insufficient fluid.

Reporting of Suspected Adverse Reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow card Scheme at www.mhra.gov.uk/yellowcard, or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

In the event of overdose, conservative measures should be taken.

Symptoms
Overdose with ispaghula husk may cause abdominal discomfort, flatulence and intestinal obstruction. Mebeverine can have neurological or cardiovascular effects in overdose.

Management
Adequate fluid intake should be maintained, and management should be symptomatic.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Alimentary tract and metabolism; Drugs for constipation; Bulk-forming laxatives; Ispaghula, combinations.

ATC Code: A06AC51

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 forty times its own weight of water in vitro and part of its activity can be attributed to its action as a simple bulking agent.

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 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

In addition, colonic bacteria are believed to use the hydrated material as a metabolic substrate. This results in an increase in the bacterial cell mass with a consequential softening of the faeces.

Mebeverine hydrochloride is a musculotropic antispasmodic agent which exerts a direct action on the smooth muscle of the gastrointestinal tract, relieving the spasm without affecting gut motility. It is rapidly absorbed with peak concentrations achieved between 1-3 hours after ingestion.

5.2 Pharmacokinetic properties

Ispaghula husk has a physical mode of action and does not depend upon absorption from the gastrointestinal tract.

The material hydrates and swells to form 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 β-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.

Mebeverine hydrochloride is mainly metabolized by esterases, initially splitting the ester bonds into veratric acid and mebeverine alcohol, which are excreted in the urine.

Mebeverine hydrochloride has been shown to be nearly completely absorbed following oral administration, but first-pass metabolism is extensive and plasma levels of unchanged drug are very low. This supports the view that it acts directly on the muscle of the gastrointestinal tract, rather than as a result of systemic absorption.

5.3 Pre-clinical Safety Data

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 to rats continuously through two generations. For fertility and foetal development and teratogenesis the no-observed-adverse-effects limit (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 cannot be drawn.

The non-clinical data on toxicology of ispaghula husk preparations are incomplete, but available data indicate no signals of toxicological concern. Adequate tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed. The reproductive toxicity of mebeverine was not sufficiently investigated in animal studies. There was no indication of teratogenic potential in rats and rabbits. However,

embryotoxic effects (reduction in litter size, increased incidence of resorption) were noticed in rats at doses equivalent to twice the maximum daily clinical dose. This effect was not observed in rabbits. No effects on male or female fertility were noted in rats at doses equivalent to the maximum clinical dose.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Basic Butylated Methacrylate Copolymer
Talc sterilised Ph Eur
Polyethylene Glycol 6000
Apocarotenal 10% WS
Citric acid
Potassium hydrogen carbonate
Sodium hydrogen carbonate
Polysorbate 80
Silica colloidal anhydrous
Orange flavour
Saccharin sodium
Beta-Carotene 10% CWS/S
Aspartame
Riboflavine sodium phosphate

6.2 Incompatibilities

None known

6.3 Shelf life

Two years

6.4 Special precautions for storage

Store below 30ºC

Store in original container

6.5 Nature and contents of container

Ten sachets of paper/aluminium foil/polythene laminate enclosed in a cardboard outer.

6.6 Special precautions for disposal

The contents of one sachet should be stirred into a glass of cold water (150ml; about ¼ pint) and taken immediately.

See Section 4.2.

7 MARKETING AUTHORISATION HOLDER

Reckitt Benckiser Healthcare (UK) Limited
Dansom Lane
Hull
HU8 7DS

8 MARKETING AUTHORISATION NUMBER(S)

PL 00063/0025

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

24/04/1995

10 DATE OF REVISION OF THE TEXT

03/02/2026