

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Fybogel Mebeverine Granules for Oral Suspension  
Ispaghula Husk 3.5g  
Mebeverine Hydrochloride 135mg.

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains:

<u>Active ingredients</u>	<u>g/sachet</u>
Ispaghula husk	3.5
Mebeverine hydrochloride	0.135

Excipients with known effect: aspartame (E951), potassium and sodium.

For the full list of excipients, see Section 6.1.

## 3 PHARMACEUTICAL FORM

Granules for oral suspension in a unit dose sachet  
Buff-coloured granules and orange-coloured spheroids.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

For the treatment of irritable bowel syndrome.

### 4.2 Posology and method of administration

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 needs to be modified for the elderly.

Children below 12: The product is not recommended in children under 12 years of age (see Section 4.4).

The product is intended for oral administration as a suspension in water (See section 4.4 Special Warnings and Precautions for Use). The product should be stirred into a glass of cold water (approx. 240 mls) and taken immediately.

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

Effects may take several 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

Patients suffering from abnormal constrictions in the gastrointestinal tract, with diseases of the oesophagus and cardia, cases of intestinal obstruction, natural or drug-induced reduction in gut motility, paralytic ileus, or faecal impaction and colonic atony such as senile megacolon.

Hypersensitivity to ispaghula husk or mebeverine (see 4.4 Special warnings and precautions for use) or to any of the excipients listed in section 6.1.

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

Undiagnosed rectal bleeding following the use of a laxative.

Failure to defecate following the use of a laxative.

Patients who have difficulty in swallowing or any throat problems.

### 4.4 Special warnings and precautions for use

Change of diet should always be considered before pharmacological management of irritable bowel syndrome. It is recommended that the use of a bulk laxative alone should be tried before using this bulk laxative/antispasmodic combined product.

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

Not recommended for children under 12.

Fybogel Mebeverine should not be taken in the dry form and should always be taken mixed with fluid (8 fluid ounces or 240 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.

Adequate fluid intake should be maintained.

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.

Ispaghula husk should not be used by patients with 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.

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.

The treatment of debilitated patients and / or elderly patients requires medical supervision.

In order to decrease the risk of gastrointestinal obstruction ispaghula husk should not be used together with medicinal products known to inhibit peristaltic movement (e.g. opioids). If deemed necessary to use this medicine with agents that inhibit peristalsis this should only be under medical supervision (see section 4.5).

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 medicinal product contains 2.50 mmol of potassium per dose. To be taken into consideration by patients with reduced kidney function or patients on a controlled potassium diet.

This medicinal product contains 2.57 mmol of sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

This medicinal product contains aspartame (E951), a source of phenylalanine. May be harmful for people with phenylketonuria.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

Ispaghula and other bulk-forming laxatives may delay or reduce the gastrointestinal absorption of other drugs such as cardiac glycosides, coumarin derivatives, lithium, carbamazepine or vitamins (such as vitamin B12) and minerals (such as calcium, iron, or zinc). 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.

Ispaghula husk should not be used together with medicinal products known to inhibit peristaltic movement (e.g. opioids) (see section 4.4). Ispaghula husk increases the water content of stools thus promoting peristalsis. If the peristaltic action of the gut is reduced, there is potential for intestinal obstruction.

#### **4.6 Fertility, pregnancy and lactation**

##### **Pregnancy:**

The product should not be used during pregnancy unless considered essential by the physician.

There are 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).

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 5.3).

##### **Breast-feeding:**

This product should not be used in breast-feeding.

Mebeverine is excreted in human milk. The excretion of mebeverine in milk has not been studied in animals.

##### **Fertility:**

There are no clinical data on male or female fertility.

#### **4.7 Effects on ability to drive and use machines**

The product has no or negligible influence on the ability to drive and use machines.

#### **4.8 Undesirable effects**

Special attention should be given to individuals manipulating the powder formulations routinely (see 4.4 Special warnings and precautions for use).

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 ( $\geq 1/10$ ); Common ( $\geq 1/100$  and  $< 1/10$ ); Uncommon ( $\geq 1/1000$  and  $< 1/100$ ); Rare ( $\geq 1/10,000$  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 <sup>1</sup>
Eye Disorders	Not known	Conjunctivitis <sup>2</sup>
Respiratory, Thoracic and Mediastinal Disorders	Not known	Rhinitis <sup>2</sup>
Gastrointestinal Disorders	Not known	Flatulence, abdominal distension, intestinal obstruction, oesophageal obstruction, faecal impaction <sup>3</sup>
Skin and Subcutaneous Tissue Disorders	Not known	Skin rash <sup>2</sup>

#### Description of Selected Adverse Reactions

<sup>1</sup> Including rash, urticaria, anaphylaxis, pruritus, and bronchospasm.

<sup>2</sup> 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.

<sup>3</sup> 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2. Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie)

## 4.9 Overdose

Symptoms:

The patient may notice abdominal discomfort and flatulence and intestinal obstruction.

#### Management:

In the event of overdosage conservative measures should be taken. Attention should be paid to maintaining an adequate fluid intake, particularly if the product has been taken without water contrary to the administration instructions.

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

### Ispaghula husk

The active ingredient ispaghula husk consists of the episperm and collapsed adjacent layers removed from the seeds of *Plantago ovate* 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 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 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

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

## **5.2 Pharmacokinetic properties**

### **Ispaghula husk**

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

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  $\beta$ -linkages, which cannot be broken by human digestive enzymes.

Less than 10% of 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**

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 its action is directly on the muscle of the gastrointestinal tract, rather than as a result of systemic absorption.

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

## 5.3 Preclinical safety data

Ispaghula husk and mebeverine hydrochloride are well-established drug substances with a known safety record.

### Ispaghula husk:

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 (multigenerational 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 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.

Tests on genotoxicity and carcinogenicity have not been performed.

### Mebeverine hydrochloride:

There is no indication of teratogenic potential in rats and rabbits exposed to mebeverine.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Citric Acid  
 Potassium Hydrogen Carbonate  
 Sodium Hydrogen Carbonate  
 Orange flavour  
 Aspartame (E951)  
 Saccharin Sodium  
 Beta Carotene (E160a) 10% CWS/S  
 Contains: Beta Carotene  
           All-*rac*- $\alpha$ -Tocopherol  
           Maize oil refined  
           Maize Starch  
           Modified food starch  
 Polysorbate 80  
 Silica, Colloidal Anhydrous  
 Riboflavine Sodium Phosphate  
 Microcrystalline cellulose  
 Basic Butylated Methacrylate Copolymer  
 Sterilised Talc  
 Macrogol  
 Apocarotenal

### 6.2 Incompatibilities

Not applicable.

### **6.3 Shelf life**

Two years.

### **6.4 Special precautions for storage**

Store below 30°C. Store in the original package.

### **6.5 Nature and contents of container**

Sachets of paper/aluminium foil/polythene laminate enclosed in a cardboard outer.  
Cartons containing 2 and 10 sachets.

Not all pack sizes may be marketed.

### **6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

See Section 4.2.

The contents of one sachet should be stirred into a glass of cold water (240mls) and taken immediately.

## **7 MARKETING AUTHORISATION HOLDER**

Reckitt Benckiser Ireland Limited  
7 Riverwalk  
Citywest Business Campus  
Dublin 24  
Ireland

## **8 MARKETING AUTHORISATION NUMBER**

PA0979/010/001

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 14 March 1986

Date of last renewal: 14 March 2006

## **10 DATE OF REVISION OF THE TEXT**

January 2017