Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Agiolax®

Granules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substances:

5 g granules (= 1 teaspoonful) contains:

Ispaghula seed 2.60 g

Ispaghula husk 0.11 g

Senna 0.34 – 0.66 g

(equivalent to 15 mg hydroxyanthracene derivatives, calculated as sennoside B).

For a full listing of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Granules

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For short-term use in constipation.

4.2. Posology and method of administration

The maximum daily dose of hydroxyanthracene derivatives is 30 mg. On average, this is equivalent to 10 g (= 2 teaspoonfuls) of **Agiolax®** granules.

Dosages for adults and children over 12 years of age:

1 to 2 teaspoonfuls **Agiolax®** granules once daily, to be taken with plenty of liquid after the evening meal.

The correct individual dose is the smallest required to produce a comfortable soft formed motion.

Mode of administration and duration of use:

The granules should be swallowed unchewed with plenty of liquid (a quarter of a litre).

When other medicinal products are used concomitantly, it is recommended to take this product 30 minutes to one hour later.

At best, **Agiolax®** should be taken in the evening. The effect occurs after 8 to 12 hours. The laxative should not be used for a longer than 1 to 2 weeks and not be taken in higher doses.

4.3 Contraindications

Hypersensitivity reactions to the active substances or any of the other ingredients. Pathological gastrointestinal tract stenosis, ileus, acute inflammatory bowel diseases, such as Crohn's disease, ulcerative colitis, appendicitis, abdominal pain of unknown origin, severe dehydration states with water and electrolyte depletion. Children under 12 years of age; patients with difficult to control diabetes mellitus.

4.4 Special warnings and precautions for use

If stimulating laxatives are taken for longer than a brief period of treatment, this may lead to aggravation of the constipation.

The product should only be used if a therapeutic effect cannot be achieved by a change in diet or the administration of bulk forming agents.

Note:

When **Agiolax®** is administered to incontinent adults, pads should be changed more frequently to prevent extended skin contact with faeces.

4.5 Interaction with other medicinal products and other forms of interaction

Due to potassium depletion, chronic use/abuse may enhance the effect of cardiac glycosides and affect the action of antiarrhythmic agents.

Combination with diuretics, adrenocorticosteroids and liquorice roots may enhance potassium depletion.

The absorption orally co-administered medicinal products may be reduced. In insulin-dependent diabetics, a reduction in the insulin dose may be required.

4.6 Pregnancy and breast-feeding

In the first three months of pregnancy **Agiolax®** should be taken only if constipation cannot be resolved by a change in diet or the administration of bulk forming agents.

Notes:

Small amount of active metabolites (such as rhein) are excreted in breast milk. A laxative effect in breast-fed babies has not been reported.

4.7 Effects on the ability to drive and use machines

Agiolax® has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The following convention has been used for the classification of side effects in terms of frequency:

Very common: ≥ 1/10

Common: ≥ 1/100 to < 1/10

Uncommon: ≥ 1/1,000 to < 1/100

Rare: ≥ 1/10,000 to < 1/1,000

Very rare: < 1/10,000

Not known: Frequency cannot be estimated from the available data.

Very rarely abdominal pain and spasm may occur. In such cases, a dose reduction is necessary. In the course of treatment, red coloration of urine may occur, which is not clinically significant.

Chronic use/abuse may lead to disorders in water equilibrium and electrolyte metabolism. Diarrhoea may especially cause potassium depletion which may lead to cardiac disorders and muscular asthenia, particularly where cardiac glycosides, diuretics and adreno-corticosteroids are being taken at the same time. Chronic use may result in albuminuria and hematuria. Furthermore, Chronic use may cause pigmentation of the intestinal mucosa (pseudomelanosis coli), which usually recedes when the patient stops taking the preparation.

Very rarely, hypersensitivity reactions to Ispaghula may occur.

Very rarely, oesophagus obstruction may be experienced.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.health.gov.il.

4.9. Overdose

Accidental or intentional overdose may cause painful intestinal spasm and severe diarrhoea with consequent losses of fluid and electrolytes as well as severe gastrointestinal discomfort.

In the package leaflet, the attention of patients is drawn to the following: In case of suspected overdosing, contact a doctor immediately. He/she will decide which counter measures (e.g., administration of fluid and salts/electrolytes) if any – are necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Laxatives

ATC code: A06AB56

Swelling and bulking agents from Ispaghula seed/husk (Indian flea seeds, Indian flea seeds husks) physiologically enhance intestinal passage by producing an increased volume of intestinal contents through their water binding capacity and bulking properties thus producing a stretch stimulus and accelerating intestinal passage. The swollen mass of mucilage softens the stools and improves gliding properties.

The action of Ispaghula drugs on colon motility is supported by Senna glucosides (sennosides) from Senna pods.

1,8-dihydroxyanthracene derivatives possess a laxative effect. In case of sennosides or their active metabolite in the large intestine (rhein anthrone) this effect is mainly based on an influence on the motility of the large intestine (stimulation of peristaltic contractions and inhibition of local contractions) resulting in accelerated colonic transit and - due to reduced contact time – in reduced fluid absorption. In addition, water and electrolytes are secreted by stimulation of the active chloride secretion. The onset of action of anthracene derivatives can be expected with a delay of approximately 8 to 12 hours.

The special pharmaceutical formulation of Ispaghula drugs and Senna pods in the form of granules allow for releasing the sennosides from **Agiolax®** in a delayed manner thus avoiding fast surge of high sennoside concentrations.

5.2 Pharmacokinetic properties

Systemic studies on the kinetics of drug preparations are not available. However, it can be expected that the aglyca contained in the drug product are absorbed in the upper gut already.

The ß-linked glycosides are prodrugs which are neither split nor absorbed in the upper gut. They are converted by bacterial enzymes of the large intestine into rhein anthrone. Rhein anthrone is the laxative metabolite. Systemic availability of rhein anthrone is extremely low. In animal experiments, less than 5% were excreted in form of the oxidised, partially conjugated products rhein and sennidines.

Most of rhein anthrone (approx. 90%) is excreted in faeces bound to the intestinal contents as polymer.

Active metabolites, e.g. rhein pass in small amounts into breast milk. A laxative effect in breast-fed babies has not been reported. Animal experiments demonstrated that placental passage of rhein is small.

5.3 Preclinical safety data

Presumably due to their aglyca content, drug preparations seem to have a higher general toxicity than purified glycosides.

An extract from Senna was mutagenic in vitro tests, the purified substances sennoside A, B gave negative results. In vivo mutagenicity examinations of a defined extract of Senna pods were negative. Study data refer to extracts containing 1.4 – 3.5% anthraquinones (calculated as the total of the individual identified compounds), corresponding to 0.9 – 2.3% potential rhein, 0.05 – 0.15% of potential aloe-emodin and 0.001 – 0.006% of potential emodin. Sometimes, positive results were obtained for aloe-emodin and emodin.

A study on carcinogenicity of senna pods in rats was conducted. Compared to the control group, oral doses of up to 300 mg/kg BW administered for 104 weeks did not lead to a higher incidence of tumour rates. The product under investigation contained 1.83 % of sennosides A-D (calculated as the total of the individual identified compounds), equivalent of approximately 1.59 % of potential total rhein determined by way of computation, 0.11 % potential aloe-emodin and 0.014 % of potential emodin.

In addition, a carcinogenicity study is available for an enriched sennosides fraction containing approximately 40.8% of anthranoides, thereof 35 % of total sennosides (calculated as the total of the individual identified compounds) equivalent to approximately 25.2% of potential total rhein determined by way of computation, 2.3% of potential aloe-emodin and 0.007% of potential emodin.

The substance investigated contained 142 ppm free aloe-emodin and 9 ppm of free emodin. In this study on rats for 104 weeks at doses up to 25 mg/kg BW, no substance related incidence of tumours was seen.

6. PHARMACEUTICAL PARTICULARS

6.1 List of other excipients

Sucrose, talc, Gum Arabic (acacia), Iron oxides (yellow, red, black), Liquid paraffin, Hard paraffin, Peppermint oil, Sage oil, Caraway oil.

1 teaspoonful contains approx. 1.05 g of sucrose (sugar), equivalent to 0.09 bread units (BU).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

After first opening of the can, **Agiolax®** can be used for 6 months.

6.4 Special precautions for storage

Do not store above 25°C *(*Can with screw-on closure*)*.

Tightly close the can after each use!

6.5 Nature and contents of container

Original packs of 100 g, 200 g brown granules (Can with screw-on closure).

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Megapharm Ltd. P.O.B 519 Hod-Hasharon 4510501

8. MARKETING AUTHORISATION NUMBER

140-20-22366

9. MANUFACTURER

Madaus GmbH D-51101 Koln, Germany

The format of this leaflet was determined by the ministry of health and its content was checked and approved in September 2015.