Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Senokot 7.5 mg/5 ml Syrup

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of Senokot Syrup contains calcium sennosides equivalent to 7.5 mg per 5ml total sennosides (calculated as sennoside B).
Ethanol (present in Prune Flavouring)
Present in the flavour at a level of 50 %. Equivalent to 6.9 mg/5 ml

Methyl Parahydroxybenzoate: 9 mg/5 ml
Propyl Parahydroxybenzoate: 2 mg/5 ml
Maltitol liquid 1.5 g/ 5 ml

For the full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Syrup.

Amber, slightly viscous liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As a laxative for the relief of occasional or non-persistent constipation.

4.2 Posology and method of administration

Senokot 7.5 mg/5 mlSyrup is for oral administration.
The correct individual dose is the smallest required to product a comfortable soft-formed motion.

Adults, including the elderly and children over 12: One to two 5 ml spoonfuls at night.

A higher dose may be prescribed under medical guidance. The maximum recommended daily dose of hydroxyanthracene glycosides is 30 mg (20 ml).

Children over 6 years: One to two 5 ml spoonfuls at night, under the guidance of a medical professional.

Children aged 2 to 6 years: Half to one 5 ml spoonful at night under the guidance of a medical professional.

New users should start with the lowest dose and increase it, if necessary, by one half of the initial dose each day. Once regularity has been regained the dosage should be gradually reduced and stopped. If no bowel action has occurred after three days of progressively increased dosage, a medical examination should be considered.

Duration of use
Normally it is sufficient to take this medicinal product up to two or three times a week. Use for more than 1-2 weeks requires medical supervision. If the symptoms persist or worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients. Not to be used the same time as other laxative agents. Cases of intestinal obstructions and stenosis, atony, appendicitis, inflammatory colon diseases (e.g. Crohn's disease, ulcerative

colitis), abdominal pain of unknown origin, severe dehydration state with water and electrolyte depletion. Children under 2 years of age.

4.4 Special warnings and precautions for use

If there is no bowel movement after three days, a doctor should be consulted. If laxatives are needed every day or abdominal pain persists, a doctor should be consulted
If laxatives are needed every day the cause of the constipation should be investigated. Long-term use of laxatives should be avoided.
Contains maltitol liquid. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Each 5 ml of syrup can provide up to 3.2 kcal and this should be taken into account in patients with diabetes mellitus.
Methyl and propyl parahydroxybenzoate may cause allergic reactions (possibly delayed).
This medicine contains 6.9 mg of alcohol (ethanol) in each 5ml dose. The amount in each dose of this medicine is equivalent to less than 1 ml beer or 1 ml wine.
The small amount of alcohol in this medicine will not have any noticeable effects.
Do not exceed the stated dose.
Patients taking cardiac glycosides, antiarrhythmic medicinal products, medicinal products inducing QT-prolongation, diuretics, adrenocorticosteroids or liquorice root have to consult a doctor before taking this product concomitantly.
Like all laxatives, this product should not be taken by patients suffering from faecal impaction and undiagnosed, acute or persistent gastro-intestinal complains, e.g. abdominal pain, nausea and vomiting, unless advised by a doctor, because these symptoms can be signs of potential or existing intestinal blockage (ileus).

If stimulant laxatives are taken for longer than a brief period of treatment, this may lead to impaired function of the intestine and dependence on laxatives. This product should only be used if a therapeutic effect cannot be achieved by a change of diet or the administration of bulk forming agents.
Prolonged use may precipitate the onset of an atonic, non-functioning colon.
Prolonged and excessive use may lead to fluid and electrolyte imbalance and hypokalaemia.
Intestinal loss of fluids may promote dehydration. Symptoms may include thirst and oliguria.
Patients with kidney disorders should be aware of possible electrolyte imbalance.
When administering this product to incontinent adults, pads should be changed more frequently to prevent extended skin contact with faeces.
Laxatives do not help in long-term weight loss.

4.5 Interaction with other medicinal products and other forms of interactions

Hypokalaemia(resulting from long-term laxative abuse) potentiates the action of cardiacglycosides and interacts with antiarrhythmic medicinal products with medicinalproducts which induce reversion to sinus rhythm (e.g. quinidine) and withmedicinal products inducing QT-prolongation. Concomitant use with othermedicinal products including hypokalaemia (e.g. diuretics,adrenocorticosteroids and liquorice root) may enhance electrolyte imbalance

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no reports of undesirable or damaging effects during pregnancy and on the foetus when used at the recommended dosage.

However, as a consequence of experimental data concerning a genotoxic risk of several anthranoids, e.g. emodin and aloe-emodin, use is not recommended in pregnancy.

Lactation
Use during breast-feeding is not recommended as there are insufficient data on the excretion of metabolites in breast milk.

Small amounts of active metabolites, such as rhein, are excreted in breast milk in small amounts. A laxative effect in breast fed babies has not been reported.

Fertility
There are no data on the effects of the product on fertility.

4.7 Effects on ability to drive and use machines

No studies on the effect of the ability to drive and use machines have been performed.

4.8 Undesirable effects

Adverse events which have been associated with sennosides at OTC doses in short-term use are given below, tabulated by system organ class and frequency. In the treatment of chronic condition, under long-term treatment, additional adverse effects may occur.

Adverse events table		
System Organ Class	**Frequency**	**Adverse Events**
Immune system disorders	Not known	Hypersensitivity, urticaria, asthma, hypogammaglobulinaemia
Metabolism and Nutrition disorders	Not known	Hypokalaemia[1], cachexia
Gastrointestinal disorders	Not known	Abdominal pain, abdominal spasm, diarrhoea[2], gastrointestinal tract mucosal pigmentation[3]
Skin and Subcutaneous Tissue Disorders	Not known	Pruritus, local or generalised exanthema
Musculoskeletal and Connective Tissue disorders	Not known	Finger clubbing, tetany and hypertrophic osteoarthropathy
Renal and Urinary disorders	Not known	Chromaturia[4]

Description of Selected Adverse Reactions

[1] Prolonged use of laxatives resulting in diarrhoea and subsequently hypokalaemia.

[2] In particular in patients with irritable colon. Symptoms may also occur generally as a consequence of individual overdosage. In such cases dose reduction is necessary.

[3] Chronic use may cause pigmentation of the intestinal mucosa (pseudomelanosis coli), which usually recedes when the patient stops taking the preparation

[4] Yellow or red-brown (pH dependent) discolouration of urine by metabolites, which is not clinically significant, may occur during the treatment.

Chronic use may lead to disorders in water equilibrium and electrolyte metabolism and may result in albuminuria and haematuria. The frequency is not known (cannot be estimated from the available data).

If other adverse reactions not mentioned above occur, a doctor or a qualified healthcare practitioner should be consulted.

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 Ireland HPRA Pharmacovigilance, Website: www.hpra.ie.

4.9 Overdose

Symptoms

Where diarrhoea is severe, conservative measures are usually sufficient; generous amounts of fluid, especially fruit drinks, should be given.

The major symptoms of overdose/abuse are griping pain and severe diarrhoea with consequent losses of fluid and electrolytes, which should be replaced. Diarrhoea may especially cause potassium depletion, which may lead to cardiac disorders and muscular asthenia, particularly where cardiac glycosides, diuretics, adrenocorticosteroids or liquorice root are being taken at the same time.

Treatment

Treatment should be supportive with generous amount of fluid. Electrolytes, especially potassium, should be monitored. This is especially important in the elderly. Chronic ingested overdoses of anthranoid containing medicinal products may lead to toxic hepatitis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: contact laxatives
ATC code: A 06 AB

The sugar moiety of the sennosides is removed by bacteria in the large intestine releasing the active anthrone fraction. This stimulates peristalsis via the submucosal and myenteric nerve plexuses.

1,8-dihydroxyanthracene derivatives possess a laxative effect. The β-O-linked glycosides (sennosides) are not absorbed in the upper gut; they are converted by bacteria of the large intestine into the active metabolite (rhein anthrone).

There are two different mechanisms of actions:

1. Stimulation of the motility of the large intestine resulting in accelerated colonic transit.
2. Influence on secretion processes by two concomitant mechanism viz. inhibition of absorption of water and electrolytes (Na+ Cl-) into the colonic epithelial cells (antiabsorptive effect) and increase of the leakiness of the tight junctions and stimulation of secretion of water and electrolytes into the lumen of the colon (secretagogue effect) resulting in enhanced concentrations of fluid and electrolytes in the lumen of the colon.

Defaecation takes place after a delay of 8-12 hours due to the time taken for transport to the colon and metabolisation into the active compound.

5.2 Pharmacokinetic properties

The action of the sennosides is colon specific and does not depend upon systemic absorption.
The β-O-linked glycosides (sennosides) are neither absorbed in the upper gut nor split by human digestive enzymes. They are converted by the bacteria of the large intestine into the active metabolite (rhein anthrone). Aglyca are absorbed in the upper gut. Animal experiments with radio-labeled rhein anthrone administered directly into the caecum demonstrated absorption <10%. In contact with oxygen, rhein anthrone is oxidised into rhein and sennidins, which can be found in the blood, mainly in the form of glucuronides and sulphates. After oral administration of sennosides, 3 - 6% of the metabolites are excreted in urine; some are excreted in bile.

Most of the sennosides (ca. 90%) are excreted in faeces as polymers (polyquinones) together with 2 - 6% of unchanged sennosides, sennidins, rhein anthrone and rhein. In human pharmacokinetic studies with senna pods powder (20 mg sennosides), administered orally for 7 days, a maximum concentration of 100 ng rhein/ml was found in the blood. An accumulation of rhein was not observed. Active metabolites, e.g. rhein, pass in small amount into breast milk. Animal experiments demonstrated that placental passage of rhein is low.

5.3 Preclinical safety data

There are no new, systematic preclinical tests for senna leaves or preparations thereof. Data derive from investigations with senna pods. Since the spectrum of constituents of senna leaf and fruit is comparable these data can be transferred to senna leaves. Most data refer to extracts of senna pods containing 1.4 to 3.5% of anthranoids, corresponding to 0.9 to 2.3% of potential rhein, 0.05 to 0.15% of potential aloe-emodin and 0.001 to 0.006% of potential emodin or isolated active constituents, e.g. rhein or senosides A and B. The acute toxicity of senna pods, specified extracts thereof, as well as of sennosides in rats and mice was low after oral treatment.

As a result of investigations with parenteral application in mice, extracts are supposed to possess a higher toxicity than purified glycosides, possibly due to the content of aglyca.

In a 90-day rat study, senna pods were administered at dose levels from 100mg/kg up to 1,500 mg/kg. The tested drug contained 1.83% sennosides A-D. 1.6% potential rhein, 0.11% potential aloe-emodin and 0.014% potential emodin. In all groups epithelial hyperplasia of the large intestine of minor degree was found and was reversible within the 8-week recovery period. The hyperplastic lesions of the forestomach epithelium were reversible as well. Dose-dependent tubular basophilia and epithelial hypertrophy of the kidneys were seen at a dose of, or greater than, 300mg/kg per day without functional affection. These changes were also reversible. Storage of a brown tubular pigment lead to a dark discolouration of the renal surface and still remained to a lesser degree after the recovery period. No alterations were seen in the colonic nervous plexus. A no-observable-effect-level (NOEL) could not be obtained in this study,

A 104-week study on rats of both genders did not reveal any carcinogenic effects with the same senna pods preparation at oral dosages of up to 300 mg/kg. In addition, a specified senna extract given orally for 2 years was not carcinogenic in male or female rats. The extract investigated contained approximately 40.8% of anthranoids from which 35% were sennosides, corresponding to about 25.2% of potential rhein, 2.3% of potential aloe-emodin and 0.007% of potential emodin and 142 ppm free aloe-emodin and 9 ppm free emodin.

Further 2-year studies on male and female rats and mice with emodin gave no evidence of carcinogenic activity for male rats and female mice, and equivocal evidence for female rats and male mice.
Senosides displayed no specific toxicity when tested at doses up to 500 mg/kg in dogs for 4 weeks and up to 100 mg/kg in rats for 6 months. There was no evidence of any embryolethal, teratogenic or foetotoxic actions in rats or rabbits after oral treatment with sennosides. Furthermore, there was no effect on the postnatal development of young rats, on rearing behaviour of dams or on male and female fertility in rats. Data for herbal preparations are not available.

An extract and aloe-emodin were mutagenic in in-vitro tests, sennoside A, B and rhein gave negative results. Comprehensive in-vivo examinations of a defined extract of senna pods were negative.

Laxative use as a risk factor in colorectal cancer (CRC) was investigated in some clinical trials. Some studies revealed a risk for CRC associated with the use of anthraquinone-containing laxatives, some studies did not. However, a risk was also revealed for constipation itself and underlying dietary habits. Further investigations are needed to assess the carcinogenic risk definitely.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Potassium sorbate E202
Methyl parahydroxybenzoate E218
Propyl parahydroxybenzoate E216
Maltitol liquid E965
Xanthan gum
Anti-foam (Medical C) emulsion
Prune flavour (ethanol)
Citric acid anhydrous
Purified water

6.2 Incompatibilities

None known.

6.3 Shelf life

Thirteen months.

6.4 Special precautions for storage

Do not store above 25°C.Do not freeze.

6.5 Nature and contents of container

Glass bottle with a polypropylene cap with a polyethylene tamper-evident band with an expanded polyethylene wad containing 100, 150 or 200 ml syrup.
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

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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

8 MARKETING AUTHORISATION NUMBER

PA0979/016/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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