SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
EX-LAX SENNA PILLS

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains sennosides, as calcium salts, equivalent to 12 mg hydroxyanthracene glycosides, calculated as sennoside B.

Each tablet contains 39.42 mg of sucrose, 26.65 mg of lactose and 1.25 mg of glucose (See Section 4.4. special warnings and precautions for use).
For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Coated tablets
Circular, biconvex, brownish red sugar coated tablets with approx. 6mm diameter

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
For the short term relief of occasional constipation.

4.2 Posology and method of administration
For oral use
Adults, the elderly and children over 12 years: 1 tablet at bedtime.
A higher dose may be prescribed by a medical practitioner. The maximum daily dose of hydroxyanthracene glycosides is 30 mg.
Normally it is sufficient to take this product up to two to three times per week.
Not recommended for children under 12 years.
Duration of use
Use for more than 7 days requires medical supervision.
A doctor should be consulted if there is no bowel movement after three days
If the symptoms persist during the use of the medicinal product, a doctor or a pharmacist should be consulted.

4.3 Contraindications

Hypersensitivity to the active ingredient or to any of the excipients listed in section 6.1.

Cases of intestinal obstructions, stenosis or atony, appendicitis inflammatory diseases of the colon (e.g. Crohn’s diseases and ulcerative colitis.).

Not to be used the same time as any other laxatives.

Irritation of the gastrointestinal tract (e.g. nausea, vomiting or colic)

Patients with ileostomy or colostomy.

Abdominal pain of unknown origin which may be due to undiagnosed underlying conditions, such as acute intestinal and/or surgical conditions (e.g. acute diverticulitis, appendicitis, and high output diarrhoea).

Severe dehydration states, with water and electrolyte depletion, especially hypokalaemia.

Children under 12 years of age

4.4 Special warnings and precautions for use

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 Ex-Lax Senna Pills concomitantly.

Like all laxatives, Ex-Lax Senna Pills should not be taken by patients suffering from faecal impaction and undiagnosed, acute or persistent gastro-intestinal complaints, 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).

Laxative preparations should only be used if a therapeutic effect cannot be achieved by a change of diet or the administration of bulk forming agents. If laxatives are needed every day the cause of the constipation should be investigated.
ExLax Senna pills should not be used for more than 7 days without medical supervision.

Prolonged indiscriminate use of laxatives may lead to habituation and impairment of intestinal function. The lowest effective dosage for the re-establishment of normal bowel function should be employed.

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. Laxatives do not help in long-term weight loss.

During use, an adequate level of fluid intake should be maintained. If no bowel action has occurred, dosage may be increased accordingly under medical supervision. If laxatives are needed every day the cause of the constipation should be investigated. Long term use of laxatives should be avoided.

When laxative preparations are administered to incontinent adults, pads should be changed more frequently to prevent extended skin contact with faeces.

Patients with kidney disorders should be aware of possible electrolyte imbalance.

Use of the medicine requires medical supervision:
- If no beneficial effects are seen following treatment
- If use exceeds one week
- If symptoms persist or become worse
- Following laparotomy or abdominal surgery
- If skin rash, nausea or vomiting are present

This product contains:
- **Sucrose**: patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
- **Lactose**: patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine
- **Glucose**: patients with rare glucose-galactose malabsorption should not take this medicine

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

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

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

Breast-feeding
Use during breastfeeding is not recommended as there are insufficient data on the excretion of metabolites in breast milk. Small amounts of active metabolites (rhein) are excreted in breast milk. A laxative effect in breastfed babies has not been reported.

Fertility
Preclinical studies with sennosides do not indicate special hazard to fertility at therapeutically relevant doses. No data are available with Senna fruit preparations.

4.7 Effects on ability to drive and use machines
This medicine has no influence on the ability to drive and use machines.

4.8 Undesirable effects
Hypersensitivity reactions (pruritus, urticaria, local or generalised exanthema) may occur.

The product may produce abdominal pain and spasm and passage of liquid stools, irritation of the stomach mucosa membrane and colon, in particular in patients with irritable colon. However, these symptoms may also occur generally as a consequence of individual overdose. In such cases dose reduction is necessary.

Other effects such as dehydration, hypotension, fatigue, myopathy, stomach pain, hyponatraemia, renal disorders, secondary hyperaldosteronism, hypocalcaemia and hypomagnesaemia have also been reported. These adverse reactions are usually reversible on laxative withdrawal.

Chronic use may lead to disorders in water equilibrium and electrolyte metabolism (e.g. hypokalaemia) and may result in albuminuria and haematuria. Furthermore, chronic use may cause pigmentation of the intestinal
mucosa (pseudomelanosis coli), which usually recedes when the patient stops taking the preparation.

Yellow or red-brown (pH dependent) discoloration of urine by metabolites, which is not clinically significant, may occur during the treatment. Habituation to the product after prolonged use has been reported.

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

**Tabulated list of adverse reactions**

Based on available data the frequency of the following adverse reactions cannot be estimated.

<table>
<thead>
<tr>
<th>System Organ Class (SOC)</th>
<th>Adverse Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metabolism and nutrition disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Frequency</td>
<td></td>
</tr>
<tr>
<td>Hyperaldosteronism</td>
<td></td>
</tr>
<tr>
<td>Hypomagnesaemia</td>
<td></td>
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<tr>
<td>Dehydration</td>
<td></td>
</tr>
<tr>
<td>Hypokalaemia</td>
<td></td>
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<tr>
<td>Blood electrolytes decreased</td>
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<tr>
<td><strong>Vascular disorders</strong></td>
<td></td>
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<tr>
<td>Not known</td>
<td></td>
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<tr>
<td>Hypotension</td>
<td></td>
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<tr>
<td><strong>Gastrointestinal disorders</strong></td>
<td></td>
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<tr>
<td>Not known</td>
<td></td>
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<tr>
<td>Megacolon</td>
<td></td>
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<tr>
<td>Abdominal pain</td>
<td></td>
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<tr>
<td>Diarrhoea</td>
<td></td>
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<tr>
<td>Nausea</td>
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<tr>
<td>Abdominal discomfort</td>
<td></td>
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<tr>
<td><strong>Musculoskeletal and connective tissue disorders</strong></td>
<td></td>
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<tr>
<td>Not known</td>
<td></td>
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<tr>
<td>Myopathy</td>
<td></td>
</tr>
<tr>
<td><strong>Renal and urinary disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Not known</td>
<td></td>
</tr>
<tr>
<td>Renal disorders</td>
<td></td>
</tr>
<tr>
<td>Chromaturia</td>
<td></td>
</tr>
</tbody>
</table>
General disorders and administration
site conditions
Not known Fatigue
Drug tolerance

Paediatric population
Frequency, type and severity of adverse reactions in children are expected to be the same as in adults.

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 (www.mhra.gov.uk/yellowcard).

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

Management
Treatment should be supportive with an increase in fluid intake to reverse the loss of fluid and electrolytes. 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: Stimulant laxative
ATC-code: A 06A B06

Mechanism of action and pharmacodynamic effects
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 action:
1. stimulation of the motility of the large intestine resulting in accelerated colonic transit.

2. influence on secretion processes by two concomitant mechanisms 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.

Sennoside laxatives generally produce bowel movement in 6 to 12 hours.

### 5.2 Pharmacokinetic properties

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 amounts into breast milk. Animal experiments demonstrated that placental passage of rhein is low.

### 5.3 Preclinical safety data

Most data refer to extracts 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 sennosides 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 100 mg/kg of 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 300 mg/kg per day without functional affection. These changes were also reversible. Storage of a brown tubular pigment led to a dark discoloration 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. Sennosides 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.

Chronic 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
Sucrose
Lactose monohydrate
Maize starch
Talc
Acacia
Titanium dioxide
Glucose
Stearic acid
Gelatin
Silica colloidal anhydrous
Red iron oxide
Carnauba wax

6.2 Incompatibilities
None known

6.3 Shelf life
36 months

6.4 Special precautions for storage
Do not store above 25°C

6.5 Nature and contents of container
Blister pack composed of PVC/PVdC blisters sealed with aluminium foil.

Pack sizes: 6, 9, 10, 12, 18, 20, 24, 30, 36, 40 or 48 tablets

6.6 Special precautions for disposal and other handling
Not applicable.

7 MARKETING AUTHORISATION HOLDER
GlaxoSmithKline Consumer Healthcare (UK) Trading Limited,
980 Great West Road
Brentford
Middlesex
TW8 9GS
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
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10 DATE OF REVISION OF THE TEXT