SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Sennosides 7.5mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains
Sennosides (as calcium salts) equivalent to 7.5mg of Hydroxyanthracene glycosides, calculated as Sennoside B.

Each tablet contains 15mg of lactose monohydrate (See Section 4.4 Special warnings and precautions for use)
For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Tablets
Brown coloured, speckled, circular, uncoated tablets debossed ‘BP’ on one side and ‘1’ on other side.
Approximate size of the tablet is 9mm (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 only
The correct individual dose is the smallest required to produce a comfortable soft-formed motion.

Adults, elderly and children over 12 years old: Two tablets taken at bedtime (Tablets should be taken as a single dose) under guidance of a medical professional.

Children over 6-12 years: One tablet to be taken at bed time.

Children under 6 years: Not recommended.
The dose should be decreased as the bowel habit becomes regular.
Duration of use
Usually it is sufficient to take this medicinal product up to two to three times a week. Use for more than 1 – 2 weeks requires medical supervision. 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 the symptoms worsen, or persist 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 at 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.

4.4 Special warnings and precautions for use
If laxatives are needed every day the cause of the constipation should be investigated. Long-term use of laxatives should be avoided.
The product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
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 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).
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.
The use in children under 6 years of age is not recommended because data are not sufficient and medical advice should be sought.
Laxatives do not help in long-term weight loss.
4.5 Interaction with other medicinal products and other forms of interaction
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. Concomitant use with other medicinal products inducing 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 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 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 on the ability to drive and use machines have been performed.

4.8 Undesirable effects
Hypersensitivity reactions (pruritis, urticaria, local or generalized exanthema) may occur.
This product may produce abdominal pain and spasm and passage of liquid stools, 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.
Chronic use may lead to disorders in water equilibrium and electrolyte metabolism and may result in albuminuria and haematuria. Furthermore, chronic use may cause pigmentation of the intestinal mucosa (pseudomelanosis coli).
Yellow or red-brown (pH dependent) discolouration of urine by metabolites, which is not clinically significant, may occur during the treatment. The frequency is not known.

**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](http://www.mhra.gov.uk/yellowcard). Yellow Card in the Google Play or Apple App Store.

### 4.9 Overdose
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 should be supportive with generous amounts of fluid. Electrolytes, especially potassium, should be monitored. This is especially important in the elderly. Chronic ingested overdose of anthranoid containing medicinal products may lead to toxic hepatitis.

### 5 PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Laxatives, Contact laxatives
ATC-code: A 06 AB

1.8-dihydroxyanthracene derivatives possess a laxative effect. The β-O-linked glycosides (senosides) 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.

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 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.

The short-term use of senna pods as recommended can be regarded as safe.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Microcrystalline Cellulose
Calcium Hydrogen Phosphate, anhydrous
Lactose Monohydrate
Maize Starch
Croscarmellose Sodium
Povidone K30
Magnesium Stearate
Maltodextrin

6.2 Incompatibilities
None known

6.3 Shelf life
36 months

6.4 Special precautions for storage
This medicinal product does not require any special storage conditions
6.5  Nature and contents of container
Aluminium PVC/PVdC blisters containing 20, 60 and 100 tablets.
Not all sizes may be marketed

6.6  Special precautions for disposal
Not applicable

7  MARKETING AUTHORISATION HOLDER
Blue Bio Pharmaceuticals Limited,
5th Floor
Beaux Lane House,
Mercer Street Lower,
Dublin 2
Ireland

8  MARKETING AUTHORISATION NUMBER(S)
PL 33831/0029

9  DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
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10  DATE OF REVISION OF THE TEXT
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