BIO-HEALTH

Cassilax

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

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1 NAME OF THE MEDICINAL PRODUCT

CASSILAX

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each coated tablet contains:
90mg Senna Leaf (*Cassia senna* L.)
15mg Aloes (Cape aloes; *Aloe ferox* Miller and its hybrids)
30mg Cascara bark (*Rhamnus purshianus* D.C.)
30mg Dandelion Root (*Taraxacum officinale* Weber ex Wigg.)

Each tablet contains 102mg of sucrose.
For full list of excipients see section 6.1

3 PHARMACEUTICAL FORM

Brown uncoated Bi-convex tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

A traditional herbal medicinal product used for the short term relief of occasional constipation and bloating, based on traditional use only.

4.2 Posology and method of administration

For oral use only.

Adults and the elderly: 1 or 2 tablets at night when required.
Not recommended for use in children and adolescents under 18 years of age (see section 4.3 Contraindications).

Duration of use:-
Use for more than 1-2 weeks requires medical supervision.
If there is no bowel movement after 3 days a doctor should be consulted.
If laxatives are needed every day, or abdominal pain persists, a doctor should be consulted.
If the symptoms persist during the use of the product, a doctor or a pharmacist should be consulted.
See also section 4.4 Special warnings and precautions for use.

4.3 Contraindications

Hypersensitivity to any of the active substances or to Apiaceae (Umbelliferae) (aniseed, caraway, celery, coriander and dill) or to anethole or to plants of the Asteraceae (Compositae) family or to any of the other ingredients.
Cases of intestinal obstructions and stenosis, atony, appendicitis, inflammatory colon diseases (e.g. Crohnís disease, ulcerative colitis) abdominal pain of unknown origin, severe dehydration state with water and electrolyte depletion.
Obstructions of bile ducts, cholangitis, liver diseases, gallstones, active peptic ulcer and any other biliary diseases.

4.4 Special Warnings and Precautions for Use

Do not exceed the stated dose.

Patients taking cardiac glycosides, antiarrhythmic medicinal products, medicinal 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, vomiting, unless advised by a doctor, because these symptoms can be signs of potential or existing intestinal blockage (ileus).

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If laxatives are needed every day the cause of the constipation should be investigated. Long term use of laxatives should be avoided. 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.

When administering this product 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.

The use in patients with renal failure and/or diabetes, and/or heart failure should be avoided because of the possible risk due to hypokalemia.

The use in children and adolescents under 18 years of age is not recommended due to lack of adequate data.

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 which induce reversion to sinus rhythm (e.g. quinidine) and with medical products inducing QT-prolongation. Concomitant use with other medical products inducing hypokalemia (e.g. diuretics, adrenocorticosteroids and liquorice root) may enhance electrolyte imbalance.

4.6 Fertitlity, Pregnancy and Lactation

Pregnancy: There are no reports of undesirable or damaging effect s during pregnancy and on the foetus when used at the recommended dose. However, experimental data show a genotoxic risk of several anthranoids, e.g. aloe-emodin, emodin, frangulin, chrysophanol and physcion, use is not recommended during pregnancy.

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

After administration of other anthranoids, active metabolites, such as rhein, are excreted in breast milk in small amounts. A laxative effect in breast fed babies has not been reported.
Studies on the effects of the product on fertility have not been performed.

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 generalised exanthema) may occur. Allergic reactions to fennel, affecting the skin or the respiratory system, 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) which usually recedes when the patient stops taking the preparation.

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

Epigastric pain and hyperacidity may occur.

The frequency of the undesirable effects is not known. If other adverse reactions not mentioned above occur, a doctor or qualified healthcare practitioner should be consulted.

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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 muscularasthenia, 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 overdoses of anthranoid containing medicinal products my lead to toxic hepatitis.ot been performed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

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

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

Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

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 (20mg 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.

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5.3 Preclinical safety data

Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

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 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 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.

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.

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6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Fennel Seeds, Gum Myrrh, Sucrose, Gum Acacia, Purified Talc, Sodium Starch Glycollate, Magnesium Stearate.

6.2 Incompatibilities

None known.

6.3 Shelf-life

3 years.

6.4 Special Precautions for storage

Store below 25°C. Store in the original package.

6.5 Nature and contents of container

100ml HDPE polythene tablet container and tamper evident cap closure. Packs contain 60 or 30 tablets.

6.6 Special precautions for disposal

There are no special precautions for disposal.

7 MARKETING AUTHORISATION HOLDER

Kerbina Limited T/A
Bio-Health Limited
Culpeper Close
Medway City Estate
Rochester
Kent. ME2 4HU

8 MARKETING AUTHORISATION NUMBER(S)

THR 00904/0004

9 DATE OF REGISTRATION

20/03/2013

10 DATE OF REVISION

20/03/2013

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