SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Napiers Herbease Laxative Tablets
Box's Herbals Radiant Laxative Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each coated tablet contains: -

45 mg of Senna leaf (Cassia senna L.)
22.5 mg of Cape Aloe leaf (Aloe ferox Miller)
15 mg of Cascara bark (Rhamnus purshiana D.C.)
15 mg of Dandelion root (Taraxacum officinale Weber ex Wigg.)
15 mg of Valerian root (Valeriana officinalis L.)
7.5 mg of Myrrh resin (Commiphora myrrha Engl.)
7.5 mg Holy Thistle herb (Cnicus benedictus L.)

Each tablet contains 72.5 mg of sucrose (see section 4.4. ‘Special warnings and precautions for use’)

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Coated tablets, pink biconvex

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
A traditional herbal medicinal product used for the short term relief of occasional constipation, based on traditional use only.
4.2 **Posology and method of administration**

For oral use only.

Adults and the elderly: One or two tablets before a meal or at bedtime.

Maximum daily dose: 2 tablets

The use in children and adolescents under 18 years of age is not recommended. (see section 4.4 ‘Special warnings and precautions for use’).

**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 ingredients 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. Crohn’s disease, ulcerative colitis) abdominal pain of unknown origin, severe dehydration state with water and electrolyte depletion.

Obstructions of bile ducts, cholangitis, liver diseases, gall stones, 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).

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 because data are insufficient and medical advice should be sought.

This product contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

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

No studies have been carried out to determine if drug interactions occur with this product.

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 medical products inducing hypokalemia (e.g. diuretics, adrenocorticosteroids and liquorice root) may enhance electrolyte imbalance.

Only limited data on pharmacological interactions of Valerian with other medicinal products are available. Clinically relevant interaction with drugs metabolised by the CYP 2D6, CYP 3A4/5, CYP 1A2 or CYP 2E1 pathway has not been observed.

Combination with synthetic sedatives is not recommended.

The effect of Valerian may be potentiated by alcohol. Excessive concomitant consumption of alcohol should therefore be avoided.
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 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**

May impair ability to drive and use machines. If affected, patients should not drive or operate machinery.

4.8 **Undesirable effects**

Hypersensitivity reactions (pruritis, urticaria, local or generalised exanthema) may occur.

Gastrointestinal symptoms (e.g. nausea, abdominal cramps) may occur after ingestion of Valerian root.

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, hyperacidity and allergic reactions may occur with Dandelion root.

The frequency of the undesirable effects is not known.

If other adverse reaction not mention above occurs, a doctor or qualified health care practitioner should be consulted.

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 overdoses of anthranoid containing medicinal products may lead to toxic hepatitis.

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-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 (secretagoguineffect) 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 metabolites are excreted in urine; some are excreted in bile.

Most of the sennosides (ca.90%) are excreted in faeces as polymrs (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 100ng 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
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
300mg/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 aloemodin and 0.007% of potential emodin and 142ppm free aloemodin 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 aloemodin were mutagenic in in vitro tests, sennosides 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
Sucrose
Acacia
Talc
Magnesium stearate
Sodium starch glycolate
Fennel seed
Kaolin light
Beetroot powder
Water
6.2  Incompatibilities
None

6.3  Shelf life
3 years

6.4  Special precautions for storage
Do not store above 25ºC. Store in the original container.

6.5  Nature and contents of container
Glass bottle with a Bakelite type screw cap closure, packed in a cardboard carton: 50, 100 and 150 tablets

Not all pack sizes may be marketed

6.6  Special precautions for disposal
There are no special precautions for disposal.

7  MARKETING AUTHORISATION HOLDER
Highland Herbs Limited
10 Payne Street
Glasgow
G4 0LF

8  MARKETING AUTHORISATION NUMBER(S)
THR 43751/0021
9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
15/04/2013

10 DATE OF REVISION OF THE TEXT
21/01/2015