Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Laxose (Lactulose Solution BP) 3.35g/5ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of solution contains 3.35 g lactulose.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution
Clear to almost clear pale yellow oral solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of hepatic encephalopathy (HE).
In the treatment of constipation.

4.2 Posology and method of administration

The lactulose solution may be administered diluted or undiluted.

A single dose of lactulose should be swallowed in one and should not be kept in the mouth for an extended period of time.
The posology should be adjusted according to the individual needs of the patient. In case of a single daily dose, this should be taken at the same time e.g. during breakfast. During the therapy with laxatives it is recommended to drink sufficient amounts of fluids (1.5 – 2 litres, equal to 6-8 glasses) during the day.

Dosing in Constipation
Lactulose may be given as a single daily dose or in two divided doses.

After a few days the starting dosage may be adjusted to the maintenance dose based upon treatment response.

Several days (2-3 days) of treatment may be needed before treatment effect occurs.

	Starting dose daily	Maintenance dose daily
Adults and adolescents	15 - 45 ml	15 – 30 ml
Children (7-14 years)	15 ml	10 – 15 ml
Children (1-6 years)	5 - 10 ml	5 – 10 ml
Infants under 1 year	Up to 5 ml	Up to 5 ml

Dosing in Hepatic encephalopathy HE (for adults only)

Starting Dose	Maintenance Dose
3 to 4 times daily 30-45 ml	Starting dose may be adjusted to the maintenance dose to achieve 2 – 3 soft stools per day

Paediatric population
The safety and efficacy in children (newborn to 18 years of age) with HE have not been established. No data is available.

Elderly patients and patients with renal or hepatic insufficiency
No special dosage recommendations exist, since systemic exposure to lactulose is negligible.

4.3 Contraindications

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

Use in patients who require a galactose-free diet.
Use in patients with evidence of gastrointestinal obstruction, gastrointestinal tract perforation or risk of gastrointestinal tract perforation.

4.4 Special warnings and precautions for use

Consultation of a physician is advised in case of:
- Painful abdominal symptoms of undetermined cause before the treatment is started
- Insufficient therapeutic effect after several days.

Patients with rare hereditary problems of fructose intolerance, the Lapp lactase deficiency, galactose intolerance, galactosaemia or glucose-galactose malabsorption should not take this medicine.

Lactulose should be administered with care to patients who are intolerant to lactose.

Chronic use of unadjusted doses and misuse can lead to diarrhoea and disturbance of the electrolyte balance.

Long term use of this product is inadvisable except under medical supervision.
The dose normally used in constipation should not pose a problem for diabetics. The dose used in the treatment of HE is usually much higher and may need to be taken into consideration for diabetics.

Paediatric population

Use of laxatives in children should be exceptional and under medical supervision.

It should be taken into account that the defecation reflex could be disturbed during the treatment.

4.5 Interaction with other medicinal products and other forms of interaction

Although lactulose could theoretically delay the intestinal release of mesalazine from modified-release preparations, a study found no evidence that lactulose influences the release or disposition of mesalazine in healthy volunteers.

4.6 Fertility, pregnancy and lactation

Fertility
No effects are to be expected, since systemic exposure to lactulose is negligible.

Pregnancy
No effects during pregnancy are anticipated, since systemic exposure to lactulose is negligible.

The product may be used during pregnancy when considered necessary by the physician.

Lactation
No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to lactulose is negligible.

The product can be used during breastfeeding

4.7 Effects on ability to drive and use machines

Laxose has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile
Flatulence may occur during the first few days of treatment. As a rule it disappears after a few days. When dosages higher than instructed are used, abdominal pain and diarrhea may occur. In such a case the dosage should be decreased.

If high doses (normally only associated with hepatic encephalopathy, HE) are used for an extended period of time, the patient may experience an electrolyte imbalance due to diarrhea.

Tabulated list of adverse reactions

The following undesirable effects have been experienced with the below indicated frequencies in lactulose-treated patients in placebo-controlled clinicial trials [very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000)].

		Frequency category		
MedDRA SOC	**Very Common**	**Common**	**Uncommon**	**Rare**
Gastrointestinal disorders	Diarrohea	Flatulence, abdominal pain, nausea, vomiting		
Investigations			Electrolyte imbalance due to diarrohea	

Paediatric population
The safety profile in children is expected to be similar 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

If the dose is too high the following may occur:

Symptom: diarrhea and abdominal pain.

Treatment: cessation of treatment or dose reduction. Extensive fluid loss by diarrhoea or vomiting may require correction of electrolyte disturbances.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Osmotically acting laxatives, ATC code: A 06A D11

In the colon, lactulose is broken down by colonic bacteria into low molecular weight organic acids. These acids lead to a lowering of pH in the colonic lumen and via an osmotic effect to an increase of the volume of the colonic contents. These effects stimulate the peristalsis of the colon and normalise the consistency of the stools. The constipation is cleared and the physiological rhythm of the colon is reinstated.

In hepatic encephalopathy (HE), the effect has been attributed to the suppression of proteolytic bacteria by an increase of acidophilic bacteria (e.g. lactobacillus), trapping of ammonia in the ionic form by acidification of the colonic contents, catharsis due to the low pH in the colon as well as an osmotic effect and the alteration of the bacterial nitrogen metabolism by stimulating the bacteria to utilise ammonia for bacterial protein synthesis. Within this context, however, it should be realised that hyperammonemia alone cannot explain the neuropsychiatric manifestations of HE. The ammonia however might serve as a model compound for other nitrogenous substances.

5.2 Pharmacokinetic properties

Lactulose is poorly absorbed after oral administration and reaches the colon unchanged where it is metabolised by the bacterial flora. Metabolism is complete at doses up to 40 - 75 ml; at higher doses, some may be excreted unchanged.

5.3 Preclinical safety data

The results of acute, sub-chronic and chronic toxicity studies in various species indicate that the compound has very low toxicity. The effects observed, appear to be more related to the effect of bulk in gastrointestinal tract than to a more specific toxic activity. In reproduction and teratology experiments in rabbits, rats or mice no adverse effects were found.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Purified Water

May contain small amounts of lactose, epilactose, galactose, tagatose and fructose.

6.2 Incompatibilities

None known.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Polyethylene bottle with polypropylene cap.
HDPE bottle with ROPP cap.
Polyethylene bottle with polypropylene cap with Polyethylene liner.
HDPE bottle with polypropylene cap with Polyethylene liner.

Pack sizes: 100 ml, 150 ml, 300 ml, 500 ml, 1 L, 2.5 L, 5 L.

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

Pinewood Laboratories Limited
Trading as Pinewood Healthcare
Ballymacarbry
Clonmel
Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0281/079/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 07 May 1996

Date of last renewal: 07 May 2006

10 DATE OF REVISION OF THE TEXT

June 2017