# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Lactulose 3.335 g/5 ml oral solution

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml of oral solution contains Lactulose 3.335 g.

Excipients with known effect: Also contains small amounts of lactose, galactose, fructose, tagatose or epilactose.

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Oral solution

Clear, viscous liquid, colourless or pale brownish yellow.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

1.) For the treatment of constipation.
2.) For the treatment of hepatic encephalopathy (HE): treatment and prevention of hepatic coma or precoma

### 4.2 Posology and method of administration

The lactulose solution may be administered diluted or undiluted. Each dose may if necessary be taken with water or fruit juices, etc.

Each 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 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.

*Lactulose oral solution in bottles:*

| | **Starting dose daily** | **Maintenance dose daily** |
|---|---|---|
| Adults and adolescents | 15-45 ml, corresponding to 10-30 g lactulose | 15-30 ml, corresponding to 10-20 g lactulose |
| | | |

| | | |
|---|---|---|
| Children<br>(7-14 years) | 15 ml, corresponding to 10 g lactulose | 10-15 ml, corresponding to 7-10 g lactulose |
| Children<br>(1-6 years) | 5-10 ml, corresponding to 3−7 g lactulose | 5-10 ml, corresponding to 3-7 g lactulose |
| Infants under 1 year | up to 5 ml, corresponding to up to 3 g lactulose | up to 5 ml, corresponding to up to 3 g lactulose |

For a precise dosing for infants and children up to 7 years lactulose in bottles should be used.

Dosing in hepatic encephalopathy (for adults only):
*Starting dose*: 3 to 4 times daily 30-45 ml (6-9 x 5 ml spoonfuls).
This dose may be adjusted to the maintenance dose to achieve two or three soft stools each day.

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

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

## 4.3 Contraindications

- Hypersensitivity to the active substance substance or to any of the excipients listed in section 6.1.
- Galactosaemia.
- Gastro-intestinal obstruction, digestive perforation or risk of digestive 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.

Long term use of this product is inadvisable except under medical supervision.

Lactulose should be administered with care to patients who are intolerant to lactose (see section 6.1).

The dose normally used in constipation should not pose a problem for diabetics. A dose of 30 ml provides 116 KJ (28 kcals) and is unlikely to adversely affect diabetics. The dose used in the treatment of hepatic encephalopathy is usually much higher and may need to be taken into consideration for diabetics.

Chronic use of unadjusted doses and misuse can lead to diarrohea and disturbance of the electrolyte balance. As diarrhoea induced by lactulose may lead to electrolyte imbalance, use with caution in patients prone to developing electrolyte disorders (e.g. patients with renal or hepatic impairment, patients receiving concomitant diuretics).

**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.

**Important information regarding the ingredients of this medicine**

This medicine contains small amounts of lactose, galactose, fructose, tagatose and epilactose. Patients with rare hereditary problems of galactose or fructose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

## 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 influenced the release or disposition of mesalazine in healthy volunteers.

## 4.6 Fertility, pregnancy and lactation

Pregnancy

No effects during pregnancy are anticipated, since systemic exposure to lactulose is negligible.
Lactulose can 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.
This medicine can be used during breast-feeding.

Fertility

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

## 4.7 Effects on ability to drive and use machines

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

## 4.8 Undesirable effects

Flatulence may occur during the first few days of treatment. As a rule it disappears after a couple of days. When dosages higher than instructed are used, abdominal pain and diarrhoea may occur. In such a case the dosage should be decreased. See also overdose section 4.9.

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 diarrhoea. Dosage should then be adjusted to obtain two or three formed stools per day.

Tabulated list of adverse reactions

The following undesirable effects have been experienced with the below indicated frequencies in lactulose-treated patients in placebo-controlled clinical 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)].

| MedDRA SOC | Frequency category | | |
|---|---|---|---|
| | **Very common** | **Common** | **Uncommon** |
| Gastrointestinal disorders | Diarrhoea | Flatulence, abdominal pain, nausea, vomiting | |
| Investigations | | | Electrolyte imbalance due to diarrhoea |

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:
Symptoms: diarrhoea and abdominal pain.
Treatment: cessation of treatment or dose reduction. Extensive fluid loss by diarrhoea or vomiting may require correction of electrolyte disturbances.
No specific antidote. Symptomatic treatment should be given.

# 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 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 colonic contents. These effects stimulate peristalsis of the colon and return the consistency of the stool. The constipation is cleared and the physiological rhythm of the colon is reinstated.
In hepatic encephalopathy (HE) the effect has been attributed to 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 alteration of the bacterial nitrogen metabolism by stimulating the bacteria to utilize ammonia for bacterial protein synthesis.

## 5.2 Pharmacokinetic properties

Lactulose is poorly absorbed after oral administration and it reaches the colon unchanged. There it is metabolised by the colonic bacterial flora. Metabolism is complete at doses up to 25-50 g or 40-75 ml; at higher dosages, a proportion 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 the 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

Lactulose does not contain any excipients, but may contain small amounts of related sugars (e.g. lactose, galactose, epilactose, fructose) from the route of synthesis.

## 6.2 Incompatibilities

Not applicable

## 6.3 Shelf life

36 months

Use within 12 months of first opening

## 6.4 Special precautions for storage

Store below 25°C.

## 6.5 Nature and contents of container

White PET bottles with polyethylene screw cap containing 100 ml,
200 ml, 300 ml, 500 ml, 1000 ml.
Polypropylene measuring cup with filling marks is supplied with each container.
Not all pack sizes may be marketed.

## 6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

# 7 MARKETING AUTHORISATION HOLDER

Bristol Laboratories Ltd,
Unit 3, Canalside,
Northbridge Road
Berkhamsted
HP4 1EG
UK

# 8 MARKETING AUTHORISATION NUMBER

PA1240/017/001

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of authorisation: 28th October 2016

## 10 DATE OF REVISION OF THE TEXT