SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lactulose Solution

Lactulose 3.35 g/5 ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Lactulose 3.35 g/5 ml.

For excipients, see 6.1. Lactulose solution may contain small amounts of related sugars (e.g. lactose, galactose, epilactose, fructose) from the route of synthesis.

3 PHARMACEUTICAL FORM

Oral Solution.
A clear or not more than slightly opalescent, viscous liquid, colourless to brownish yellow

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of constipation

For the treatment of hepatic encephalopathy (HE); hepatic coma.

4.2 Posology and method of administration

Posology
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.

	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 HE (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.

Method of Administration
Oral use

Special populations
Paediatric population:
The safety and efficacy in children (newborn to 18 years of age) with hepatic encephalopathy (HE) have not been established. No data are 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 any of the ingredients listed in section 6.1.
- Galactosaemia.
- Gastro-intestinal obstruction, perforation or risk of perforation.

4.4 Special warnings and precautions for use

Painful abdominal symptoms of undetermined cause should be evaluated to exclude undiagnosed perforation or obstruction or undiagnosed disease/condition that predisposes to either before the treatment is started.

In case of insufficient therapeutic effect after several days the dose and/or additional measures should be re-considered.

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

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

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.

Information on related sugars from the route of synthesis with known effect:
This product may contain small amounts of lactose, galactose and fructose from the route of synthesis. Therefore, patients with rare hereditary problems of galactose or fructose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Lactulose should be administered with care to patients who are intolerant to lactose (see section 6.1 List of excipients).

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

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Lactulose Solution can be used during pregnancy.

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

Lactulose Solution 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)];
not known (frequency cannot be estimated from the available data).

MedDRA SOC	**Frequency category**				
	Very common	**Common**	**Uncommon**	**Rare**	**Not Known**
Gastrointestinal	Diarrhoea	Flatulence,			

disorders		abdominal pain, nausea, vomiting			
Investigations			Electrolyte imbalance due to diarrhoea		
Immune system disorders					Hypersensitivity reactions
Skin and subcutaneous tissue disorders					Rash*, pruritus*, urticaria*

*Post-marketing experience

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 authorization 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 or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

If the dose is too high, the following may occur:

Symptom: diarrhoea, loss of electrolytes 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

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactulose Solution 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

None.

6.3 Shelf life

4 years (HDPE bottles)
3 years (PET bottles)

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Lactulose Solution are packed in:

- White HDPE bottles containing 300ml, 500ml, or
- PET bottles 300ml.

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

Crescent Pharma Limited
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8 MARKETING AUTHORISATION NUMBER(S)

PL 20416/0399

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

06 April 2010

10 DATE OF REVISION OF THE TEXT

05/09/2024