SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lactulose 3.3g/5ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Lactulose Solution Ph. Eur 100%, containing 66% w/v lactulose

3 PHARMACEUTICAL FORM

Solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For treatment of constipation and hepatic encephalopathy (HE); hepatic coma.

4.2 Posology and method of administration

Lactulose may be taken with water or fruit juice.

Each dose 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.

Lactulose may be given as a single daily dose or in two divided doses. In case of a single daily dose, this should be taken at the same time, e.g. during breakfast.

During therapy with laxatives it is recommended to drink sufficient amounts of fluids (1.5-2 litres, equal to 6-8 glasses) during the day.

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

Route of administration: Oral

Initial dosage for constipation:	Adults – 15ml twice daily Children 5 to 10 years –10ml twice daily Children under 5 years –5ml twice daily Babies under 1 year – 2.5ml twice daily
Initial dosage for hepatic encephalopathy:	Adults (including the elderly) – 30 to 50ml three times daily Children – no dosage recommendations for this indication.

A doctor may wish to change these initial doses as ideally two or three soft stools should be produced daily.

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 insufficiency
No special dosage recommendations exist, since systemic exposure to lactulose is negligible.

4.3 Contraindications

Lactulose Solution should not be given to patients with:

- hypersensitivity to the active substance or any of the related sugars listed in section 6.1
- gastro-intestinal obstruction, digestive perforation or risk of digestive perforation
- galactosaemia

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.

Lactulose should be administered with care to patients who are intolerant to lactose (see section 'List of excipients').
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.

Chronic use of unadjusted doses and misuse can lead to diarrhoea and disturbance of the electrolyte balance.
This product contains lactose, galactose and small amounts of fructose. Patients with rare hereditary problems of galactose or fructose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Paediatric population
Use of laxatives in children should be exceptional and under medical supervision. It should be taken into account that the defaecation reflex could be disturbed during the treatment.

4.5 Interaction with other medicinal products and other forms of interaction

None known.

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.

Lactation
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 or 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) 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:
The frequencies of adverse reactions are ranked according to the following convention: Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1000).

MedDRA SOC	**Frequency category**				
	Very common	**Common**	**Uncommon**	**Rare**	**Not known**
Gastrointestinal disorders	Diarrhoea	Flatulence, abdominal pain, nausea, vomiting			
Investigations	-	-	Electrolyte imbalance due to diarrhoea		
Immune system disorders					Hypersensitivity reactions
Skin and subcutaneous tissue disorders					Rash, pruritus, urticaria

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard .

4.9 Overdose

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

Lactulose is a synthetic disaccharide which is broken down by colonic bacteria mainly into acetic and lactic acids. These acids lead to a lowering of pH in the colonic lumen and exert a local osmotic effect in the colon resulting in increased faecal bulk and stimulation of peristalsis. The constipation is cleared and physiological rhythm of the colon is reinstated.

When larger doses are given for hepatic encephalopathy 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 utilise 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 25-50g or 40-75ml; at higher doses, 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

None known

6.3 Shelf life

3 years unopened.

6 months after first opening.

6.4 Special precautions for storage

Do not refrigerate or freeze.

6.5 Nature and contents of container

HDPE bottle with white HDPE screw cap, containing 200, 300, 500, 1000 or 5000ml of Lactulose Solution.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Relax Ltd
Level 3, Skyparks Business Centre,
Malta International Airport plc,
Luqa
LQA 4000
Malta

8 MARKETING AUTHORISATION NUMBER(S)

PL 44027/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12/07/1995

10 DATE OF REVISION OF THE TEXT

10/06/2022