Summary of Product Characteristics

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1. NAME OF THE MEDICINAL PRODUCT
RAPIDUCE (Lactulose Solution USP).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 5 ml contains
Lactulose Concentrate equivalent to Lactulose ……. 3.35 g
Aqueous base …….. q.s.
Colour: Caramel.

3. PHARMACEUTICAL FORM:
Oral solution.

Description
A clear light brownish yellow solution.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
RAPIDUCE Solution is indicated:

- In adults and children for the treatment of constipation.
- In adults for the treatment of hepatic encephalopathy (HE); hepatic coma.

4.2 Posology and method of administration
This solution may be administered diluted or undiluted.
If necessary, each dose may be taken with water or fruit juices.
Complete dose should be swallowed at once and not be kept in the mouth for an extended period of time. 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 to 2 litres) 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. Few days of treatment (2 to 3 days) may be needed before treatment effect occurs.

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

Dosing in Hepatic Encephalopathy (Adults)
Starting dose: 30 to 45 ml 3 to 4 times daily. This dose may be adjusted to the maintenance dose to achieve two or three soft stools each day.

Paediatric Population:
The safety and efficacy of lactulose solution in children (0 to 18 years of age) in hepatic encephalopathy (HE) have not been established. However, lactulose solution can be administered in paediatric patients for treating constipation.

4.3 Contraindications:
RAPIDUCE Solution is contraindicated in the following:

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

4.4 Special warnings and precautions for use
Before the treatment is started, painful abdominal symptoms of undetermined cause should be evaluated to exclude undiagnosed perforation or obstruction or undiagnosed disease/condition.
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.
This product may contain lactose, galactose, and fructose from the route of production. Therefore, patients with rare hereditary problems of galactose or fructose intolerance, the 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.

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 of lactulose is negligible

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

Fertility
No effects are to be expected, since systemic exposure of 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. However, 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.
If high doses (required for 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 clinical trials and during post-marketing experience:
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**	**Not known**
Gastrointestinal disorders		Diarrhoea	Flatulence, abdominal pain, nausea, vomiting	
Investigations			Electrolyte imbalance due to diarrhoea	
Immune system disorders				Hypersensitvity reactions
Skin and subcutaneous tissue disorders				Rash*, pruritis*, 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 national reporting system.

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4.9 Overdose
Symptom: If the dose is too high, the following symptoms may occur: 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 is available. In the case of overdose, symptomatic treatment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Osmotically acting laxative; **ATC Code:** A06AD11.

Mechanism of Action

In Constipation

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

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.

Pharmacodynamic Effects

Lactulose is used in preventing and treating clinical hepatic encephalopathy. It is also a laxative for the treatment of chronic constipation. Its osmotic effect and effect on intestinal motility leads to its therapeutic efficacy in constipation.

5.2 Pharmacokinetic properties

Lactulose, also known as 1,4 beta galactoside-fructose, is a non-absorbable synthetic disaccharide made up of galactose and fructose. The human small intestinal mucosa does not have the enzymes to split lactulose, and hence lactulose reaches the large bowel unchanged. Lactulose is metabolized in the colon by colonic bacteria to monosaccharides, and then to volatile fatty acids, hydrogen, and methane. Metabolism is complete at doses up to 25 to 50 g or 40 to 75 ml; at higher dosages, a proportion maybe 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

Caramel, Purified Water.

6.2 Incompatibilities

Not known.

6.3 Shelf life

24 Months.

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C. Do not freeze.
Keep out of reach of children.

6.5 Nature and contents of container

100 ml solution filled in amber coloured, round, PET bottle with ROPP cap and a measuring cup packed in a carton with pack insert.

6.6 Special precautions for disposal and other handling

No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Registered office :

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8. MARKETING AUTHORISATION NUMBER(S)

Certificate No: 07911/08152/NMR/2020

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Oct 9, 2022

10. DATE OF REVISION OF THE TEXT

September 2023