Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Lactulose Fresenius 670mg/ml oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml contains 670 mg Lactulose (as lactulose liquid).

3 PHARMACEUTICAL FORM

Oral solution
Clear colourless to pale brownish yellow, viscous solution

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

• Symptomatic treatment of Constipation

• Treatment of portal systemic encephalopathy

Lactulose Fresenius is indicated in adults and for constipation only in children and adolescents aged 1 month to 18 years.

4.2 Posology and method of administration

Posology
The posology should be adjusted according to the individual needs of the patient. The starting dose can be adjusted after adequate treatment effect individually (maintenance dose). Several days (2-3 days) of treatment may be needed in some patients before adequate treatment effect occurs. In case of single daily dose, this should be taken at the same time of the day, e.g. during breakfast. During the therapy with laxatives it is recommended to drink sufficient amounts of fluids (1.5-2 l/day, equal to 6-8 glasses).

Constipation

	Starting dose		Maintenance dose	
Adults	15 - 45 ml	corresponding to 10 - 30 g lactulose	15 - 30 ml	corresponding to 10 - 20 g lactulose

Paediatric population

	Starting dose		Maintenance dose	
Adolescents over 14 years	15 - 45 ml	corresponding to 10 - 30 g lactulose	15 - 30 ml	corresponding to 10 - 20 g lactulose
Children (7-14 years)	15 ml	corresponding to 10 g lactulose	10 - 15 ml	corresponding to 7 - 10 g lactulose
Children (1-6 years)	5 - 10 ml	corresponding to 3 - 7 g lactulose		
Babies	up to 5 ml	corresponding to up to 3 g		

		lactulose	

If diarrhoea occurs, the dosing regimen should be reduced.

Treatment of portal systemic encephalopathy - for adults only:

Beginning with 30 - 50 ml 3times daily (corresponding to 60 - 100 g Lactulose daily).
The dosage has to be adopted to get 2-3 soft stools daily, pH of the stools should be between 5.0 to 5.5.

In elderly patients and patients with renal or hepatic insufficiency no special dosage recommendations exist.

Paediatric Population:
The safety and efficacy of Lactulose Fresenius in children aged 0 - 18 years have not been established. No data are available.

Method of administration
The lactulose solution may be administered diluted or undiluted. The dose should be titrated according to the clinical response.
Lactulose may be given as a single daily dose or up to three divided daily doses, using the measuring cup.
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 duration of treatment has to be adopted according to the symptoms.

4.3 Contraindications

– Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
– Use in patients with galactosaemia.
– Acute inflammatory bowel disease (ulcerative colitis, Crohn's disease), gastrointestinal obstruction or subocclusive syndromes, digestive perforation or risk of digestive perforation, painful abdominal syndromes of undetermined cause.

4.4 Special warnings and precautions for use

In case of insufficient therapeutic effect after several days consultation of a physician is advised.
From the route of synthesis Lactulose Fresenius may contain traces of sugars (Not more than 67 mg/ml lactose, 100 mg/ml galactose, 67 mg/ml epilactose, 27 mg/ml tagatose and 7 mg/ml fructose). Lactulose should be administered with care to patients who are intolerant to lactose.
The dose normally used in constipation should not pose a problem for diabetics.
However, higher doses used for treatment of portal systemic encephalopathy may need to be taken into considerations for diabetics. 15 ml of Lactulose contain 42.7 KJ (10.2 kcals) = 0.21 bu.

The defecation reflex may be altered during the treatment with lactulose.
Patients with rare hereditary problems of galactose or fructose intolerance, lactase deficiency or glucose-galactose mal-absorption should not take this medicine.

For patients with gastro-cardiac syndrome (Roemheld syndrome) lactulose should only be taken after consultation of a physician. If symptoms like meteorism or bloating occur in such patients after lactulose intake, the dose should be reduced or the treatment should be discontinued.

Chronic use of unadjusted doses and misuse can lead to diarrhoea and disturbance of the electrolyte balance.
For elderly patients or patients that are in bad general condition and take lactulose for a more than 6 months period, periodic control of electrolytes is indicated.

In patients with portal systemic encephalopathy, concomitant administration of other laxatives should be avoided, because it hinders the individualization of drug dose. Furthermore, for the patients referred above, it should be taken into account the chance of causing electrolyte imbalance and, mainly, hypokalaemia that could aggravate encephalopathy.

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

Paediatric population
Use of laxatives in children should be exceptional and under medical supervision.
Lactulose should be administrated with caution in infants and small children with autosomal recessive hereditary fructose intolerance.

4.5 Interaction with other medicinal products and other forms of interactions

Lactulose may increase the loss of potassium induced by other drugs (e.g. thiazides, steroids and amphothericin B).
Concomitant use of cardiac glycosides can increase the effect of the glycosides through potassium deficiency.
With increasing dosage a decrease of pH-value in the colon is found. Therefore drugs which are released in the colon pH-dependently (e.g. 5-ASA) can be inactivated.

4.6 Fertility, pregnancy and lactation

Pregnancy
Limited data on pregnant patients indicate no malformative nor foeto/neonatal toxicity. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3).
The use of lactulose may be considered during pregnancy if necessary.

Breastfeeding
Lactulose Fresenius can be used during breastfeeding.

Fertility
For Lactulose Fresenius no clinical data on the effects on fertility are available.

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.

Gastrointestinal disorders
Very common (≥ 1/10): Flatulence, abdominal pain,
Common (≥ 1/100 < 1/10): Nausea and vomiting; if dosed too high, diarrhoea.

Immune system disorders
Not known (frequency cannot be estimated from the available data): Hypersensitivity reactions

Skin and subcutaneous tissue disorders
Not known (frequency cannot be estimated from the available data): Rash, pruritus, urticaria

Investigations
Electrolyte imbalance due to diarrhoea.

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: diarrhoea 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: Drugs for constipation. Osmotically acting laxatives, ATC code: A06A D11

Lactulose is a synthetic disaccharide formed from D-galactose and fructose. In the colon lactulose is metabolised by bacterial enzymes to short chained fatty acids mainly lactic and acetic acid as well as methane and hydrogen. This effect leads to a decrease of the pH-value and an increase of the osmotic pressure in the colon. This causes stimulation of peristalsis and an increase of the water content of the faeces.
Lactulose as a prebiotic substance strengthens the growth of bifidobacteria and lactobacilli, whereas clostridium and Escherichia coli may be suppressed.

In higher dosage lactulose causes a reduction of the pH-value, which results in an increased H^+-concentration and a shift from NH_3 (absorbable) to NH_4^+ (non-absorbable). The nitrogen excretion in the stool is accelerated. This effect may be used in the treatment of hyperammonaemia. In the treatment of hepatic encephalopathy lactulose reduces the concentration of NH_3 in the blood by about 25 - 50 %.

Lower pH in the colon leads to suppression of proteolytic bacteria, which are involved in the formation of ammonia. Decrease in pH is caused by increasing the content of acidophilic bacteria (e.g. Lactobacillus). Reduced pH and the osmotic effect cleanse the colon; this stimulates the bacteria to use ammonia for bacterial protein synthesis.

5.2 Pharmacokinetic properties

Lactulose is practically not absorbed, because in man there is no corresponding disaccharidase available in the upper intestinal tract. Not being absorbed as such, 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

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years
After first opening: 1 year

6.4 Special precautions for storage

Do not store above 25°C.
Keep container tightly closed.
For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Brown glass bottles (Ph.Eur., type III) and brown PET-bottles containing 100 ml, 200 ml, 250 ml, 300 ml, 500 ml and 1000 ml, 10 x (100 ml, 200 ml, 250 ml, 300 ml, 500 ml) and 6 x 1000 ml with a polyethylene screw cap or a polypropylene child resistant closure.
White PET-bottles containing 100 ml, 200 ml, 300 ml, 500 ml and 1000 ml, 10 x (100 ml, 200 ml, 300 ml, 500 ml) and 6 x 1000 ml with a polyethylene screw cap or a polypropylene child resistant closure.
For the bottles as measuring device a measuring cup (polypropylene) with filling marks is added.
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

Fresenius Kabi Austria GmbH
Hafnerstrasse 36
8055 Graz
Austria

8 MARKETING AUTHORISATION NUMBER

PA0773/003/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26th November 2010
Date of last renewal: 3rd February 2013

10 DATE OF REVISION OF THE TEXT

June 2022