Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Lactulose Resolution 3.3g /5ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

5ml of Lactulose solution contains 3.3 g of Lactulose
For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Oral Solution.
Clear, colourless or pale brownish yellow liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

(1) In the treatment of constipation.
(2) In the treatment of hepatic encephalopathy (portal systemic encephalopathy); hepatic coma.

4.2 Posology and method of administration

Route of administration: Oral
The recommended dosage has to be adapted to the need of the patient.
Lactulose may be taken with water or fruit juice.

Initial dosage for constipation:
Adults – 15ml twice daily
Children 5 to 10 years –10ml twice daily
Children 2 to 5 years –5ml twice daily
Babies 1 -2 year – 2.5 – 5ml twice daily
Babies 1 month - 1 year. 2.5ml twice daily

Initial dosage for hepatic encephalopathy:
Adults (including the elderly) – 30 to 50ml three times daily

Children:

The safety and efficacy in children aged 0 - 18 years has not been established. No data are available.

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

Subsequently adjust the dose to produce two or three soft stools each day.

Because of the physiological mode of action of Lactulose Liquid Ph. Eur. it may take up to 48 hours before effects are obtained. As treatment takes effect it may be possible for the patient to reduce the effective dose gradually over a period of time.

4.3 Contraindications

Lactulose Liquid should not be given to patients with

- Hypersensitivity to the active substance(s) or to any of the excipients.
- Evidence of gastrointestinal obstruction
- Galactosaemia

4.4 Special warnings and precautions for use

Each 5 ml of Lactulose solution contains not more than 0.53g of Galactose and not more than 0.40g of lactose.

Patients with the rare hereditary illnesses of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption and hereditary fructose intolerance should not take this medicine.

Lactulose should be administered with caution in infants and small children with autosomal recessive hereditary fructose intolerance.

The compound should not be used in acute inflammatory bowel disease and disturbances of water and electrolyte balances.

In patients with hepatic encephalopathy, concomitant administration of other laxatives should be avoided, because it hinders the individualization of the 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.

For elderly patients or patients that are in a bad general condition and who take lactulose for a more than 6 months period, periodic control of electrolytes is indicated.

If the constipation does not respond to treatment after a couple of days or reoccurs after treatment, a physician should be consulted.

The defecation reflex may be altered during the treatment of lactulose.

Use of laxatives in children should be under medical supervision.

During the therapy with laxatives it is recommended to drink sufficient amounts of fluids (1.5-2.1/day, equal to 6-8 glasses).

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

Lactulose should be administered with care to patients who are intolerant to lactose.

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 unajusted doses and misuse can lead to diarrhoea and disturbance of the electrolyte balance.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been conducted.

Lactulose can increase the loss of potassium induced by other active substances (e.g. diuretics, corticosteroids and

amphotericin B).

Concomitant use of cardiac glycosides may enhance the effect of the glycosides due to 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

Reports on the clinical experience of lactulose and data from animal reproduction studies have not revealed any increase in embryotoxic hazard to the foetus if used in the recommended dose during pregnancy. If drug therapy is needed in pregnancy the use of this drug is acceptable. Lactulose can be used during lactation.

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

Gastrointestinal disorders
Very common (≥ 1/10): Mild abdominal pain, meteorism, flatulence at the beginning of the treatment.
Common (≥1/100, <1/10): Nausea, vomiting, diarrhoea at higher dosage levels.

Metabolism and nutrition disorders
Rare (≥1/10,000, <1/1,000): Hypernatriaemia in the therapy of portal systemic encephalopathy.

The usual disturbances in water and electrolyte balance associated with laxatives have to be taken into account if dosages regularly producing thin stools are administered over a prolonged period of time.

4.9 Overdose

The symptoms of overdose are diarrhoea and loss of electrolytes.
No specific antidote. Symptomatic treatment should be given.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code A06 AD11
Lactulose is a synthetic disaccharide which is used in the treatment of constipation and in hepatic encephalopathy. Lactulose is broken down by colonic bacteria mainly into acetic and lactic acids which exert a local osmotic effect in the colon resulting in increased faecal bulk and stimulation of peristalsis. It may take up to 48 hours before an effect is obtained. When larger doses are given for hepatic encephalopathy the pH in the colon is reduced significantly by this acid production and the absorption of ammonium ions and other toxic nitrogenous compounds is decreased leading to a fall in blood-ammonia concentration.

5.2 Pharmacokinetic properties

Following oral administration, a negligible amount of Lactulose is absorbed in the gastro-intestinal tract. It passes essentially unchanged into the large intestine where it is metabolized by saccharolytic bacteria, forming simple organic acids such as lactic and acetic acid. Urinary excretion has been reported to be 3% or less.

5.3 Preclinical safety data

Preclinical studies based on studies of single and repeated dose toxicity reveal no special hazards for humans.

The effects observed, appear to be more related to the effect of bulk in gastrointestinal tract than to a more specific toxic activity.

A long-term animal study does not give reference to tumorigenic potential.
Lactulose was not teratogenic in mice, rats and rabbits.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water

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 store above 25°C

Do not refrigerate or freeze

6.5 Nature and contents of container

White or Natural HDPE bottle with white HDPE screw cap, with or without push -on graduated measuring cup, containing 200, 300, 500 or 1000 ml of Lactulose Solution.

Natural HDPE container with white HDPE screw cap, containing 5000ml of Lactulose Solution.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Resolution Chemicals Ltd
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Herts
SG1 4QT
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8 MARKETING AUTHORISATION NUMBER

PA1569/1/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

April 2011