Product Summary

1. Trade Name of the Medicinal Product

Lactulose Solution BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of solution contains Lactulose 3.35 g.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution.

A clear, viscous liquid, colourless or pale brownish yellow, miscible with water.

Clinical Particulars

4.1. Therapeutic Indications

Constipation, hepatic encephalopathy (portal systemic encephalopathy).

4.2 Posology and method of administration

For oral administration only
May be mixed with fruit juice, water or milk to increase palatability

Constipation
Adults: initially 15ml twice daily. Dosage can often be gradually reduced to 10-20ml a day or every other day

Starting dose
Children 5 to 10 years: 10ml twice daily
Children under 5 years: 5ml twice daily
Babies: 2.5ml twice daily

Elderly: lactulose has been shown to be a suitable laxative for use in the elderly at the standard adult dose

Hepatic encephalopathy
Adults: initially 30 – 50ml (6 – 10 x 5ml spoonfuls) three times daily
Dosage should be adjusted to produce two or three soft stools daily and an acidic faecal pH

Elderly: the standard adult dose is recommended

Children: not recommended

Because of the physiological mode of action of lactulose it may take up to 48 hours before effects are obtained. However, clinical experience has shown that this medicament does exhibit a "carry-over" effect which may enable the patient to reduce the effective dose gradually over a period of time.

4.3. Contra-indications

- Hypersensitivity to the active substance or any of the ingredients
- Galactosaemia
- Gastrointestinal obstruction, digestive perforation or risk of digestive perforation

4.4. Special Warnings and Precautions for Use

Dependence/Tolerance: Lactulose Solution does not lead to dependence, and increased tolerance is not a problem. Prolonged use of this product is not recommended except under medical supervision. The product contains a small amount of lactose (0.3 g/5 ml), therefore it should be used with caution in patients who are lactose intolerant.

A maintenance dose of 15 ml per day provides only 58 kJ (14 cals) and is therefore, unlikely to adversely affect diabetics.

Long term use of this product is inadvisable except under medical supervision.

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 Hepatic Encephalopathy 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 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. Interactions with other Medicaments and other forms of Interaction

The elimination of certain colonic bacteria by broad spectrum anti-infective agents may interfere with the degradation of lactulose and prevent the acidification of colonic contents.

4.6 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 breastfeeding woman to lactulose is negligible. Lactulose solution can be used during pregnancy.

Fertility
No effects are to be expected, since systemic exposure to lactulose is negligible.

4.7. Effects on Ability to Drive and Use Machines

Based on the pharmacodynamics of lactulose, it is unlikely that any adverse effects will occur.

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 the event of diarrhoea, adequate fluid intake should be maintained during treatment and the dosage reduced to prevent loss of fluid and potassium, and exacerbation of encephalopathy. 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)]

MedDRA SOC	Frequency Category			
	Very Common	Common	Uncommon	Rare
Gastrointestinal disorders	Diarrhoea	Flatulence, abdominal pain, nausea, vomiting		
Investigations			Electrolyte imbalance due to diarrhoea	

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

There is little information on accidental overdose. It is expected that diarrhoea and abdominal cramps would be major symptoms. There is no specific antidote and symptomatic treatment should be given if required.

5.1. Pharmacodynamic properties

A06A D11 – Osmotically acting laxatives

Lactulose is a synthetic disaccharide analogue of lactose. There is no enzyme in the gastro-intestinal area capable of hydrolysing this disaccharide. In the colon lactulose is broken down by the colonic bacteria to low molecular weight acids that produce an increased osmotic pressure and slightly acidify the colonic contents, resulting in an increase in stool water and stool softening.

Furthermore since the colonic contents are then more acid than blood, ammonia can be expected to migrate from the blood into the colon. In the acidic environment NH3 is converted to $(NH4)^+$, trapping it and preventing its absorption. This is what makes lactulose useful in hepatic encephalopathy.

5.2. Pharmacokinetic Properties

Given orally, only small amounts reach the blood, urinary excretion has been determined to be 3% or less, and is virtually complete within 24 hours.

Lactulose does not exert its effects until it reaches the colon. Therefore 24 to 48 hours may be required to produce normal bowel movement.

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 Summary of Product Characteristics.

6.1. List of excipients

No added excipients. Lactulose Solution BP may however contain the following related substances:

Galactose	nmt 15.0% of the lactulose content	(0.5025g/5ml)

Lactose	nmt 10.0% of the lactulose content	(0.335g/5ml)
Epilactose	nmt 10.0% of the lactulose content	(0.335g/5ml)
Tagatose	nmt 4.0% of the lactulose content	(0.134g/5ml)
Fructose	nmt 1.0% of the lactulose content	(0.0335g/5ml)

6.2. Incompatibilities

None known.

6.3. Shelf Life

2 years.

6.4. Special Precautions for Storage

Do not store above 25°C. Do not refrigerate or freeze. Store in the original container.

Dilution and subsequent storage not recommended.

6.5. Nature and contents of container

Amber glass bottles with plastic screw caps of 200 ml, 300 ml and 500 ml.

HDPE bottles with plastic screw caps of 200 ml, 300 ml, 500 ml, 1000 ml and 5000 ml.

Not all pack sizes may be marketed.

6.6. Instruction for Use/Handling

No special instructions.

7. MARKETING AUTHORISATION HOLDER

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Trading as: Co-pharma

8. Marketing Authorisation Number

PL 13606/0084

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15/01/2011

10 DATE OF REVISION OF THE TEXT

27/04/2017