

Summary of Product Characteristics (SmPC)

Lactulose

1 Name of the medicinal product

Duphalac[®], Bifiteral[®], Bifikral[®], Betulac[®], Gel-ose[®], Lactogel[®], Lactikralin[®].

2 Qualitative and quantitative composition

Tradename[®] liquid is an aqueous solution containing 67 g lactulose per 100 ml.

3 Pharmaceutical form

Solution for oral administration (Tradename[®] liquid)

4 Clinical particulars

4.1 Therapeutic indications

- Constipation: regulation of the physiological rhythm of the colon
- Where a soft stool is considered of medical benefit (haemorrhoids, post colon/anal surgery)
- Portal systemic encephalopathy (PSE): treatment and prevention of hepatic coma or precoma
- Salmonellosis

4.2 Posology and method of administration

The daily dosage should be adapted on individual basis. The following serves as a guideline:

In constipation or where a soft stool is considered of medical benefit

	<i>Tradename[®] liquid</i>	
	Starting dose	Maintenance dose
Adults	10-45 ml	10-25 ml
Children (7-14 years)	15 ml	10-15 ml
Children 1-6 (1-6 years)	5-10 ml	5-10 ml
Babies	5 ml	5 ml

As a rule the dosage can be decreased after a couple of days to serve patients needs.

The dosage should preferably be taken in one time during breakfast. Onset of the clinical effect may take a couple of days. This is inherent to the mode of action of lactulose. Higher dosages can be considered if a positive response has not occurred after the first two days.

Precoma and coma hepaticum

Starting dose: 3 times daily 30-50 ml
Maintenance dose: should be adapted as such that soft stools are produced maximally 2-3 times per day. The pH of the stools should be preferably 5.0-5.5

Salmonellosis

Adults:

1st course: 15 ml, 3 times daily for the duration of 10-12 days. Discontinuation for 1 week, without treatment.
2nd course: 15 ml, 5 times daily for the duration of 10-12 days. Discontinuation for 1 week, without treatment.
3rd course (if necessary): 30 ml, 3 times daily for the duration of 10-12 days.

Children:

Babies and children up to 6 years should be treated with 5 ml 4 times daily for 10-12 days. For second and third courses, the dosage should be adapted individually.

4.3 Contra-indications

- Galactosaemia
- Bowel obstruction
- Hypersensitivity to any of the components of the product

4.4 Special warnings and special precautions for use

Should the constipation not react to treatment after a couple of days or reoccur after treatment, then a physician should be consulted.

If used by lactose intolerant patients, then the lactose content (see 6.1) should be taken into consideration.

The dose normally used in constipation should not pose a problem for diabetics. The dosage used in the treatment of (pre)coma hepaticum is usually much higher and may need to be taken into consideration for diabetics.

4.5 Interactions with other medicaments and other forms of interaction

Due to lactulose's mode of action of lowering the pH in the colon, drugs that have a colon pH dependent release (such as 5-ASA agents) may be inactivated.

4.6 Pregnancy and lactation

This medicine may, on the basis of current knowledge, be safely used as instructed during pregnancy and lactation.

4.7 Effect on ability to drive and to use machines

Tradename[®] does not influence the ability to drive or to operate 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, belly ache and diarrhoea may occur. In such a case the dosage should be decreased.

If high doses (normally only associated with PSE) are used for an extended period of time, the patient may experience an electrolyte imbalance due to diarrhoea.

4.9 Overdose

No data on cases of overdosing are available. If dosed too high, belly ache and diarrhoea can occur. In such instance, cessation of treatment will normally suffice.

5 Pharmacological properties

5.1 Pharmacodynamic properties

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 the colonic contents. These effects stimulate the peristalsis of the colon and normalise the consistency of the stools. The constipation is cleared and the physiological rhythm of the colon is reinstated.

In portal systemic encephalopathy (PSE) c.q. (pre)coma hepaticum, 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. Within this context, however, it should be realized that hyperammonia alone cannot explain the neuropsychiatric manifestations of PSE. The ammonia however might serve as a model compound for other nitrogenous substances.

5.2 Pharmacokinetic properties

Lactulose is scantily absorbed after oral administration. 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 40-75 ml; at higher dosages, a part 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.

6 Pharmaceutical particulars

6.1 List of excipients

Tradename[®] liquid do not contain any excipients.

Apart from lactulose, Tradename[®] liquid contains the related sugars galactose (up to 1.5g/15ml) and lactose (up to 0.9g/15ml).

6.2 Incompatibilities

No incompatibilities with other products are known.

6.3 Shelf-life

The shelf-life of Tradename[®] liquid is 3 years when stored at temperatures not exceeding 25 °C or 2 years when stored at temperatures not exceeding 30 °C, if kept in the original undamaged package.

6.4 Special precautions for storage

Tradename[®] liquid should be stored protected from direct sunlight and preferably above 10 °C.

6.5 Nature and contents of container

Tradename[®] liquid:

Sachets, containing 15 ml are made of a polyester/aluminium/polyethylene laminate.

Containers of HDPE with polypropylene closures with a polypropylene measuring cup.

6.6 Instructions for use/handling

None.