

SUMMARY OF PRODUCT CHARACTERISTICS
Lactulose

1 NAME OF THE MEDICINAL PRODUCT

Duphalac Fruit, 667 g/l, syrup

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Duphalac Fruit, 667 g/l, syrup

Duphalac Fruit syrup contains 667 g lactulose per 1000 ml flavoured with plum aroma.

3 PHARMACEUTICAL FORM

Syrup flavoured with plum aroma.

A clear, viscous liquid, colourless to brownish yellow

APPROVED BY SCDMTE...

Expert / Date *dl/08.10.18*

Applicant / Date *dl 10.10.18*

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 colonic/anal surgery).
- Hepatic encephalopathy (HE): treatment and prevention of hepatic coma or precoma.

4.2 Posology and Method of Administration

The lactulose solution may be administered diluted or undiluted.

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 posology should be adjusted according to the individual needs of the patient.

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 – 2 liters, equal to 6-8 glasses) during the day.

For Trademark in bottles the measuring cup may be used.

Dosing in constipation or where a soft stool is considered of medical benefit Lactulose may be given as a single daily dose or in two divided doses, for Trademark in bottles the measuring cup may be used.

After a few days, the starting dosage may be adjusted to the maintenance dose based upon treatment response. Several days (2-3 days) of treatment may be needed before treatment effect occurs.

	Starting dose	Maintenance dose daily
Adults and adolescents	10-30 grams	10-20 grams
Children (7-14 years)	10 grams	7-10 grams
Children (1-6 years)	3-7 grams	3-7 grams
Infants under 1 year	up to 3 grams	up to 3 grams

For a precise dosing for infants and children up to 7 years Trademark in bottles should be used.

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Dosing in HE (for adults only)

For oral administration:

Starting dose: 3 to 4 times daily 20-30 g (2-3 sachets) or 30-45 ml (2-3 sachets).

This dose may be adjusted to the maintenance dose to achieve 2 to 3 soft stools per day.

For rectal administration:

In acute cases (impending coma or coma stage) Trademark may be administered as a retention enema (300ml Trademark/700ml water). The enema is to be retained for 30-60 minutes; the procedure is to be repeated every 4-6 hrs until oral medication can be administered.

Elderly patients and patients with renal or hepatic insufficiency

No special dosage recommendations exist, since systemic exposure to lactulose is negligible.

Children.

Use the laxatives means that children should occur in exceptional cases and requires medical supervision.

Be aware that reflex emptying can be broken in the course of treatment.

Lactulose should be used with caution in newborns and children with hereditary fructose intolerance, transmitted in an autosomal recessive manner.

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4.3 Contraindications

- Hypersensitivity to the active ingredient or to (one of) the excipients listed in section 6.1.
- Galactosaemia.
- Gastrointestinal obstruction, perforation in the digestive organs or risk of this (for example, acute inflammatory diseases of the intestine, such as colitis ulcerosa, Crohn's disease).

4.4 Special Warnings and Precautions for Use

It is advised that a doctor should be consulted in case of:

- painful abdominal symptoms of unknown origin before the treatment is started.
- insufficient therapeutic effect after a few days.

Lactulose should be given with caution to patients with a lactose intolerance (see section 6.1).

The usual dosage in constipation does normally not pose a problem for diabetics. The dosage used in the treatment of portal systemic encephalopathy is usually much higher and may need to be taken into consideration with diabetics.

This product contains lactose, galactose and small quantities of fructose. Patients with rare hereditary conditions such as galactose or fructose intolerance, Lapp-lactase deficiency or glucose-galactose malabsorption should not use this medicinal product.

When administered as a retention enema, due to the strong cathartic effect, fecal incontinence, bedsoiling, and peri-anal irritation due to the acidic stool can be expected. The hydration status of the patient should be observed carefully.

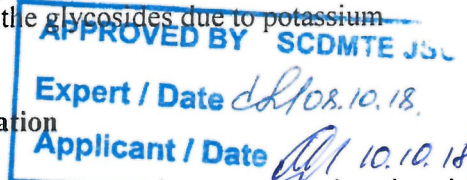
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Patients with a gastro-cardiac syndrome (Roemheld syndrome) should use lactulose only after consulting a doctor. If symptoms such as meteorism or distension occur in these patients after taking lactulose, the dosage should be reduced or treatment should be discontinued. Chronic use of unregulated doses and abuse may 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 carried out.

Lactulose may increase the potassium loss induced by other medicinal products (for example thiazides, corticosteroids and amphotericin B). Concomitant use of cardiac glycosides may increase the effect of the glycosides due to potassium deficiency.



4.6 Fertility, Pregnancy and Lactation

Pregnancy

No effects are anticipated during pregnancy, since the systemic exposure to lactulose is negligible. Lactulose syrup can be used during pregnancy (see section 5.3).

Lactation

No harmful effects on the health of the child during breastfeeding are anticipated, since the systemic exposure to lactulose is negligible.

Lactulose syrup can be during breastfeeding (see section 5.3).

Fertility

No effects are anticipated because the systemic exposure to lactulose is negligible.

4.7 Effects on Ability to Drive and Use Machines

Lactulose syrup has no or a negligible effect on the ability to drive or use machines.

4.8 Undesirable Effects

Summary of the safety profile

Flatulence may occur during the first few days of treatment. This usually disappears after a few days.

If the dosage given is higher than prescribed, abdominal pain and diarrhoea may occur. The dosage should then be reduced.

If high doses (normally only for portal systemic encephalopathy, PSE) are used for an extended period, the patient's electrolyte balance may be disturbed as a result of diarrhoea.

Table of undesirable effects

The following side effects have been observed with the frequencies indicated below in patients treated with lactulose in placebo-controlled clinical trials [very common ($\geq 1/10$); common ($\geq 1/100$, $< 1/10$); uncommon ($\geq 1/1,000$, $< 1/100$); rare ($\geq 1/10,000$, $< 1/1,000$); very rare $< 1/10,000$].

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System/ organ class	Frequency category			
	Very common	Common	Uncommon	Rare
Gastrointestinal disorders	Diarrhoea	Flatulence Abdominal pain Nausea, Vomiting		
Examinations			Disturbed electrolyte balance as a result of diarrhoea	

Paediatric patients

The safety profile is expected to be the same in children as in adults.

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4.9 Overdose

If the dose is too high, the following may occur:
Symptom: diarrhea and abdominal pain.

Treatment: cessation of treatment or dose reduction. Extensive fluid loss by diarrhea or vomiting may require correction of electrolyte disturbances.

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Osmotic laxatives, ATC-code: A06AD11

In the colon lactulose is converted by the intestinal flora into low-molecular organic acids. These acids lead to a lowering of the pH in the colonic lumen and, via an osmotic effect, to an increase in the volume of the colonic contents. These effects stimulate peristalsis of the colon and normalise faecal consistency. Constipation is relieved and the physiological rhythm of the colon is restored.

In portal systemic encephalopathy (PSE) or hepatic (pre)coma, lactulose causes a decrease in the ammonia content of the blood. The higher dosage used in this indication results in a lower pH in the colon. The growth of proteolytic bacteria is consequently inhibited, resulting in reduced production of ammonia and other toxins.

At this lower pH a high percentage of ammonia is also converted into ionised ammonia, which passes through the colon wall with difficulty. The ability of ammonia to be absorbed is consequently reduced. As a result of the lowered pH, ammonia additionally diffuses from the blood towards the colonic lumen. The effect is additionally reinforced by the generally accelerated passage time in the colon. Protein tolerance is increased by this change in ammonia metabolism. Within this context it is important to realise that hyperammonaemia alone cannot explain the neuropsychiatric manifestations of PSE.

As a prebiotic substance, lactulose intensifies the growth of Bifidobacterium and Lactobacillus, while Clostridium and Escherichia coli may be suppressed. This may lead to alleviation of the constipation and, in this way, have a favourable effect on the patient's state of health.

5.2 Pharmacokinetic Properties

Lactulose is poorly absorbed after oral administration and it reaches the colon unchanged. There it is

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metabolised by the colonic bacterial flora. Metabolism is complete at doses up to 25-50 g or 40-75 ml; at higher doses, a proportion may be excreted unchanged.

5.3 Preclinical Safety Data

The results of acute, sub-chronic and chronic toxicity studies in various species of animals indicate very low toxicity. The effects observed appear to be related more to the effect of bulk in the gastrointestinal tract than to a more specific toxic activity. No adverse effects were found in reproduction and teratology experiments in rabbits, rats and mice.

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Duphalac Fruit, 667 g/l, syrup contains plum aroma and no further excipients.

Duphalac Fruit, 667 g/l, syrup may contain small amounts of related sugars (e.g. lactose, galactose, epilactose, fructose) from the route of synthesis.

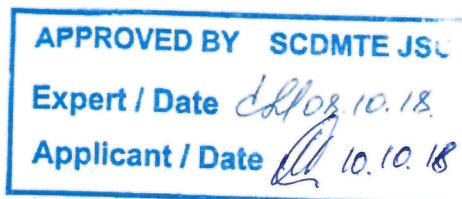
6.2 Incompatibilities

Not applicable

6.3 Shelf Life

3 years

Shelf-life after first use of HDPE bottle: 21 weeks



6.4 Special Precautions for Storage

Store at temperatures not above 25 ° C away from children.

6.5 Nature and Contents of Container

HDPE or glass bottles containing 200 ml and 500 ml.

6.6 Special Precautions for Disposal

Not applicable

MANUFACTURER

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