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.

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	15-45 ml	15-30 ml
Children (7-14 years)	15 ml	10-15 ml

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Children (1-6 years)	5-10 ml	5-10 ml
Infants under 1 year	up to 5 ml	up to 5 ml

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

Dosing in HE (for adults only)
For oral administration:
Starting dose: 3 to 4 times daily 30-45 ml.
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.
The safety and efficacy in children (newborn to 18 years of age) have not been established.
No data are available.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the ingredients.
- Galactosaemia
- Gastrointestinal obstruction, digestive perforation or risk of digestive perforation
- Trademark solution for bowel cleansing should not be administered to unconscious patients or those with impaired consciousness and patients prone to aspiration or regurgitation, general weakness, with severe dehydration or impaired swallowing reflex.

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.

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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.

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 diarrhea and disturbance of the electrolyte balance.
Sulphites may rarely cause severe hypersensitivity reactions including bronchospasm.
Pediatric population
Use of laxatives in children should be exceptional and under medical supervision.
It should be taken into account that the defecation reflex could be disturbed during the treatment.

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

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period, the patient's electrolyte balance may be disturbed as a result of diarrhoea.

Hypersensitivity reactions mainly limited to the skin have been observed and identified as potential adverse reactions during postapproval use. Because these reactions were reported spontaneously from a population of uncertain size, it is not possible to reliably estimate their frequency.

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 (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1,000); very rare <1/10,000)].

System/ organ class	**Frequency category**			
	Very common	**Common**	**Uncommon**	**Frequency not known**
Immune system disorders				Hypersensitivity
Gastrointestinal disorders	Diarrhoea	Flatulence abdominal pain nausea, vomiting		
Skin and subcutaneous tissue disorders				Rash, pruritus, urticaria, erythema
Investigations			Electrolyte imbalance due to diarrhoea	

Pediatric patients

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

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 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 return the consistency of the stools. The constipation is cleared, and the physiological rhythm of the colon is reinstated.

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 favorable 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 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

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MANUFACTURER

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