

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Duphalac 3.335 g/5 ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Lactulose solution containing 3.335 g of lactulose per 5 ml.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral solution.

Clear, colourless to pale brownish – yellow viscous liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Constipation

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 a 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 litres, equal to 6-8 glasses) during the day.

For Duphalac in bottles the measuring cup may be used.

Dosing in Constipation

Lactulose may be given as a single daily dose or in two divided doses; for Duphalac 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 daily	Maintenance dose daily
Adults and adolescents	15 – 45 ml	15 – 30 ml
Children (7-14 years)	15 ml	10 – 15 ml
Children (1-6 years)	5 – 10 ml	5 – 10 ml
Infants under 1 year	Up to 5 ml	Up to 5 ml

Dosing in Hepatic encephalopathyHE (for adults only)

Starting Dose	Maintenance Dose
3 to 4 times daily 30-45 ml	Starting dose may be adjusted to the maintenance dose to achieve 2 – 3 soft stools per day

Paediatric population

The safety and efficacy in children (newborn to 18 years of age) with HE have not been established. No data is available.

Elderly patients and patients with renal or hepatic insufficiency

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

4.3 Contraindications

Hypersensitivity to the active substance or to any of the ingredients.

Galactosaemia.

Gastrointestinal obstruction, gastrointestinal tract perforation or risk of gastrointestinal tract perforation.

4.4 Special warnings and precautions for use

Painful abdominal symptoms of undetermined cause should be evaluated to exclude undiagnosed perforation or obstruction or undiagnosed disease/condition that predisposes to either before the treatment is started.

In case of insufficient therapeutic effect after several days the dose and/or additional measures should be re-considered.

Duphalac should be administered with care to patients who are intolerant to lactose (see section 6.1).

The dose normally used in constipation should not pose a problem for diabetics. The dose used in the treatment of HE 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.

It should be taken into account that the defecation reflex could be disturbed during the treatment.

This product contains lactose, galactose and small amounts of fructose. Therefore, patients with the rare hereditary problem of galactose or fructose 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.

4.5 Interaction with other medicinal products and other forms of interaction

Although lactulose could theoretically delay the intestinal release of mesalazine from modified-release preparations, a study found no evidence that lactulose influenced the release or disposition of mesalazine in healthy volunteers.

4.6 Fertility, pregnancy and lactation**Fertility**

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

Pregnancy

No effects during pregnancy are anticipated, since systemic exposure to lactulose is negligible.

Duphalac can be used during pregnancy when considered necessary by the physician.

Lactation

No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to lactulose is negligible.

Duphalac can be used during breastfeeding.

4.7 Effects on ability to drive and use machines

Duphalac has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects**Summary of the safety profile**

Flatulence may occur during the first few days of treatment. As a rule it disappears after a few days. When dosages higher than instructed are used, abdominal pain and diarrhea may occur. In such a case the dosage should be decreased.

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 diarrhea.

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 ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

If the dose is too high the following may occur:

Symptom: diarrhoea, loss of electrolytes and abdominal pain.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Osmotically acting laxatives,
ATC code: A 06A D11

In the colon, lactulose is broken down by colonic bacteria into low molecular weight 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 hepatic encephalopathy (HE), the effect has been attributed to the 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 the alteration of the bacterial nitrogen metabolism by stimulating the bacteria to utilise ammonia for bacterial protein synthesis. Within this context, however, it should be realised that hyperammonemia alone cannot explain the neuropsychiatric manifestations of HE. The ammonia however might serve as a model compound for other nitrogenous substances.

5.2 Pharmacokinetic properties

Lactulose is poorly absorbed after oral administration and reaches the colon unchanged where it is metabolised by the bacterial flora. Metabolism is complete at doses up to 40 - 75 ml; at higher doses, some 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 gastrointestinal tract than to a more specific toxic activity. In reproduction and teratology experiments in rabbits, rats or mice no adverse effects were found.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Duphalac does not contain any excipients, but may contain sugars (e.g. lactose, galactose, fructose) and sulfite from the route of synthesis.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Three years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Opaque white multidose bottles of HDPE with a polypropylene screw cap containing 300 or 1000 ml, with a polypropylene measuring cup.

The graduations on the measuring cup are: 2.5ml, 5ml, 10ml, 15ml, 20ml, 25ml and 30ml.

Not all pack sizes may be marketed

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Mylan IRE Healthcare Limited
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8 MARKETING AUTHORISATION NUMBER

PA2010/009/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 April 1983

Date of last renewal: 01 April 2008

10 DATE OF REVISION OF THE TEXT

August 2018