Duphalac®
667 mg/ml, oral solution
667 mg/ml lactulose

Read all of this leaflet carefully before you start taking this medicine. Keep this leaflet. You may need to read it again. If you have any further questions, please ask your doctor or pharmacist. This medicine has been prescribed to you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

Duphalac is a clear, viscous, colourless to brownish yellow aqueous solution (liquid) for oral administration containing 667 g lactulose per 1000 ml. Duphalac oral solution does not contain any excipients, but may contain small amounts of related sugars (e.g. lactose, galactose, epilactose, fructose) derived from the route of synthesis.

Indications
- Constipation: regulation of the colonic physiological rhythm
- When soft stool is considered of medical benefit (haemorrhoids, post colonic/anal surgery)
- Hepatic encephalopathy (HE): treatment and prevention of hepatic coma or precoma

Dosage and administration
Always take Duphalac oral solution exactly as your doctor has told you. If you have any questions, you should check with your doctor or pharmacist.

You may take Duphalac oral solution diluted or undiluted. Take your dose of lactulose in one swallow; do not hold the solution in your mouth for any length of time.

Your doctor will adjust the dosage according to your response to the medicine. If you have been prescribed a single daily dose, always take it at the same time of day, e.g. during breakfast.

During therapy with laxatives it is important for you to drink sufficient amounts of fluids (1.5 – 2 litres, equal to 6-8 glasses) during the day.

Dosing in constipation or where soft stool is considered of medical benefit:
Duphalac may be taken as a single daily dose or in two divided doses. Your doctor will tell you which frequency to use.

For Duphalac: in a bottle, use the measuring cup may be used.

Based upon treatment response your doctor may adjust the starting dose to the maintenance dose after a few days. Several (2–3) days of treatment may be needed before treatment effect occurs.

<table>
<thead>
<tr>
<th>Duphalac oral solution</th>
<th>Starting dose daily</th>
<th>Maintenance dose daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and adolescents</td>
<td>15 - 45 ml</td>
<td>15 - 30 ml</td>
</tr>
<tr>
<td>Children (7 - 14 years)</td>
<td>15 ml</td>
<td>10 - 15 ml</td>
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<tr>
<td>Children (1 - 6 years)</td>
<td>5 - 10 ml</td>
<td>5 - 10 ml</td>
</tr>
<tr>
<td>Infants under 1 year</td>
<td>up to 5 ml</td>
<td>up to 5 ml</td>
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</tbody>
</table>

Dosing in HE (for adults only):
Starting dose: 3 to 4 times daily 30–45 ml
The dose should be adjusted by your doctor to the maintenance dose to achieve 2 to 3 soft stools per day.

Paediatric population
The safety and efficacy in children (new born to 18 years of age) with HE have not been established. No data are available.

Elderly patients and patients with renal or hepatic insufficiency. No special dosage recommendations exist, since systemic exposure to lactulose is negligible.

Contraindications
- Do not take Duphalac oral solution if you suffer from gastrointestinal obstruction, digestive perforation or risk of digestive perforation.
- Do not take Duphalac oral solution if you suffer from galactosaemia.
- Do not take Duphalac oral solution if you are hypersensitive (allergic) to lactose or to any of the ingredients of Duphalac oral solution.

Warnings and special precautions for use
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.
- If the desired results are not observed after several days of treatment, consult your doctor. Patients who are intolerant to lactose should take Duphalac oral solution with care (because it contains lactose, see section Important information about the ingredients).

The dose normally used in constipation should not pose a problem for diabetics. However, the dose used in the treatment of HE is usually much higher and should be taken into consideration for diabetics.

Chronic use of unadjusted doses and misuse can lead to diarrhoea and disturbance of the electrolyte balance.

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.

You may want to take protective measures, such as using diapers, for your small child.

This product contains lactose, galactose and small amounts of fructose. Therefore, patients with the rare hereditary problems of galactose or fructose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Interactions
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines including medicines obtained without a prescription.

No interaction studies with other medications have been performed.

Pregnancy and lactation
Ask your doctor or pharmacist for advice before taking any medicine.

Pregnancy
During pregnancy, no effects to the fetus are anticipated, since systemic exposure of lactulose to the pregnant woman is negligible.

Duphalac can be used during pregnancy.

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

Duphalac oral solution can be used during breastfeeding.

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Fertility
No effect is too expected, since systemic exposure to lactulose is negligible.

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

Important information about the ingredients
Duphalac oral solution contains lactose monohydrate. If you have been told by your doctor that you have an intolerance to some sugars, especially lactose, contact your doctor before taking this medicinal product.

Undesirable effects
Like all medicines, Duphalac oral solution may cause side effects, although not everyone experiences them. If you notice any side effects not mentioned in this leaflet, or if any of the side effects gets serious, please inform your doctor or pharmacist.

Summary of the safety profile
Flatulence may occur during the first few days of treatment. As a rule, it disappears after a few days. Diarrhoea and abdominal pain may be experienced if you take a higher dose than instructed. If this occurs, the dosage should be decreased to reflect the recommended dosage (see section Overdose). If you are taking a high dose (normally only with hepatic encephalopathy HE) for an extended period of time, you may experience an electrolyte imbalance (not enough electrolytes in your blood) due to diarrhoea.

### MedDRA SOC

<table>
<thead>
<tr>
<th>Frequency category</th>
<th>Very common</th>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal disorders</td>
<td>Diarrhea</td>
<td>Flatulence, abdominal pain, nausea, vomiting</td>
<td>Electrolyte imbalance due to diarrhea</td>
<td></td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Paediatric population
The safety profile in children is expected to be similar as in adults.

Overdose
If you have taken too high a dose you may experience the following symptoms: diarrhoea and/or abdominal pain. Under these circumstances, the treatment should be stopped or the dosage reduced sufficiently for the symptoms to subside. Extensive fluid loss (dehydration) secondary to diarrhoea or vomiting may require the intake of extra electrolytes. Please ask your doctor or pharmacist for advice.

Pharmacodynamics
Pharmacotherapeutic group: Osmotically acting laxatives, ATC Code: A06A D11
The following is a detailed description of how Duphalac oral solution works. If you would like an explanation or further information regarding this information, please consult your doctor.

In the colon lactulose is broken down by colonic bacteria into low-molecular organic acids. These acids lower the pH in the colonic lumen and increase the volume of the colonic contents via an osmotic effect. These effects stimulate peristalsis of the colon and return normal consistency of the stool. Constipation is corrected and the physiological rhythm of the colon is reinstated.

In hepatic encephalopathy (HE), 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 bacterial nitrogen metabolism by stimulating the bacteria to utilize ammonia for bacterial protein synthesis. Within this context, however, it should be realized that hyperammonemia alone cannot explain the neuropsychiatric manifestations of HE. The ammonia might, however, serve as a model compound for other nitrogenous substances.

Lactulose as a prebiotic substance strengthens the growth of health promoting bacteria, like Bifidobacterium and Lactobacillus, whereas potentially pathogenic bacteria, like Clostridium and Escherichia coli may be suppressed. This may lead to a more favorable balance of the intestinal flora.

Pharmacokinetics
The following is a detailed description of how Duphalac oral solution is metabolized in the body. If you would like an explanation or further information regarding this information, please consult your doctor.

Lactulose is poorly absorbed after oral administration and 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 dosages, a proportion may be excreted unchanged.

Incompatibilities
Not applicable.

Shelf life and storage conditions
2 years.
Do not store above 30°C.
Do not use this medicine after the expiry date stated on the carton and stick or bottle.
Keep this medicine out of the reach and sight of children.

Pack sizes
Duphalac oral solution comes in
- 10 or 20 sticks per pack with 15ml per stick. The sticks are made of a polyester/aluminium/polyethylene laminate.
- In 5 litre bottles, which are made of HDPE with HDPE closures.
- in 200, 300, 500, 800 or 1000 ml which are made of HDPE with polypropylene closures and come with a polypropylene measuring cup.

Presentations
Not all pack sizes may be marketed.

Further information
No special requirements.
The information in this leaflet is limited. For further information, please contact your doctor or pharmacist.

Date of information
March 2015

Manufactured by
Abbott Biologicals B.V.,
The Netherlands