LACTULOSE

LILAC®

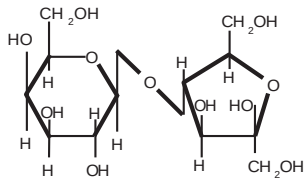
3.35g/5mL Syrup

Laxative / Cathartic

DESCRIPTION

Lactulose (Lilac®) syrup, containing lactulose with other sugars such as galactose and lactose, is used in the treatment of constipation and hepatic encephalopathy.

Lactulose is a disaccharide; a sugar molecule composed of two smaller sugar molecules bonded together, in this case fructose and galactose. Lactulose is a solid substance that is very soluble in water and has a sweet taste. Lactulose is a colonic acidifier which promotes laxation. Chemically lactulose is also known as 4-O-β-D-galactopyranosyl-D-fructofuranose. The molecular formula is $C_{12}H_{22}O_{11}$ and the structural formula is:



Lactulose

FORMULATION

Lactulose (Lilac®) is available for oral administration as:

Lactulose (Lilac®) Syrup
Each 5mL contains:
Lactulose USP … 3.35g
(together with other sugars such as galactose and lactose)

CLINICAL PHARMACOLOGY

Mechanism of Action

Two mechanisms are believed to be involved in the laxative action of lactulose: 1) Metabolism of lactulose by bacteria results in reduced colonic pH, which stimulates peristalsis and decreases stool transit time. In turn, decreased water reabsorption from the feces further facilitates the passage of soft, well formed stools. 2) Increased osmotic pressure of fecal material secondary to an increase in colonic organic acids results in accumulation of fluid from surrounding tissues, helping to soften stool mass. The therapeutic action of lactulose in ameliorating the symptoms of hepatic encephalopathy is considered to be a result of the following:

- Reduction of fecal pH leading to reduced ammonia absorption via non-ionic diffusion and/or diffusion of ammonia from the blood into the gut. The trapped ammonia is then excreted in the stools.
- Suppression of urase producing organisms.
- Induction of an osmotic type of diarrhea, which diminishes fecal statis with reduction of nitrogenous substances for ammonia production. Decreased absorption of ammonia from the gut also results from shortening intestinal transit time.

The actual mechanism may be a combination of these effects.

Pharmacokinetics

Lactulose is poorly absorbed from the gastrointestinal tract and no enzyme capable of hydrolysis of this disaccharide is present in human gastrointestinal tissue.

Following administration by mouth, lactulose passes essentially unchanged into the large intestine where it is metabolised by saccharolytic bacteria with the formation of simple organic acids, mainly lactic acid and small amounts of acetic and formic acids.

The small amount of absorbed lactulose is subsequently excreted unchanged in the urine. Urinary excretion has been determined to be 3% or less and is essentially complete within 24 hours.

INDICATIONS

Lactulose (Lilac®) is indicated for the treatment of:

- Constipation.
- Portal systemic encephalopathy (hepatic encephalopathy) including stages of hepatic pre-coma and coma.

DOSAGE AND ADMINISTRATION

Lactulose (Lilac®) is taken orally. The dosages specified here are meant as a guideline only and must always be adjusted to meet the individual requirements of the patient depending on severity and development of the symptoms. Each dose may, if necessary, be taken with water or fruit juices, etc.

Constipation:

	Starting dose (per day)
Adults (including the elderly)	15mL twice daily
Children (5-10 years)	10mL twice daily
Children (under 5 years)	5mL twice daily
Infants (under 1 year)	2.5mL twice daily

24-48 hours maybe required to produce a normal bowel movement.

Portal Systemic Encephalopathy:

Adults (including elderly): Initially dose of 30 – 50mL three to four times a day. The dose is subsequently adjusted to produce 2 or 3 soft stools each daily.

ADVERSE EFFECTS

Lactulose may cause abdominal discomfort associated with flatulence or cramps. Nausea and vomiting have occasionally been reported after high doses. Prolonged use or excessive dosage may result in diarrhea with excessive loss of water and electrolytes, particularly potassium.

CONTRAINDICATIONS

Lactulose is contraindicated in:

- Patients who require a low galactose diet.
- Patients with galactosaemia or disaccharide deficiency.
- Patients with intestinal obstruction.

PRECAUTIONS

General

- Those who develop gastrointestinal symptoms (flatus, bloating, and diarrhea) with the use of dietary fiber should exercise caution in the use of lactulose.
- Care should be taken in patients who are lactose intolerant.
- Lactulose syrup contains galactose and lactose and should be used with caution in diabetics as blood glucose levels may be elevated, usually after extended use.
- In the overall management of portal-systemic encephalopathy, it should be recognized that there is serious underlying liver disease with complications such as electrolyte disturbance (e.g., hypokalemia) for which other specific therapy may be required. Hypernatremia has been reported.
- Infants receiving lactulose may develop dehydration.

Laboratory Tests

Elderly, debilitated patients who receive lactulose for more than six months should have serum electrolytes (potassium, chloride, carbon dioxide) measured periodically.

Pregnancy:
There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Nursing Mothers:
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when lactulose solution is administered to a nursing woman.

Drug Interactions:
- Theoretically, the elimination of certain colonic bacteria by neomycin and possibly other anti-infective agents may interfere with the desired degradation of lactulose and thus prevent the acidification of colonic contents. Thus the status of the lactulose-treated patient should be closely monitored in the event of concomitant oral anti-infective therapy.
- Results of preliminary studies suggest that nonabsorbable antacids given concurrently with lactulose may inhibit the desired lactulose-induced drop in colonic pH. Therefore, a possible lack of desired effect of treatment should be taken into consideration before such drugs are given concomitantly with lactulose.
- Other laxatives should not be used, especially during the initial phase of therapy for portal-systemic encephalopathy because the loose stools resulting from their use may falsely suggest that adequate lactulose dosage has been achieved.

STORAGE
Store at temperatures not exceeding 30°C.
Do not refrigerate or freeze.
Protect from light.
The expiration date refers to the product correctly stored at the required conditions.

Under recommended storage conditions a normal darkening of colour may occur. Such darkening is characteristic of sugar solutions and does not affect therapeutic efficacy.

Keep out of reach of children.

AVAILABILITY
Lactulose (Lilac®) syrup is available in an amber-coloured bottles of 60mL and 120mL.

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to FDA: www.fda.gov.ph

REGISTRATION NUMBER
DR-XY28642 (Under Getz Pharma)
DR-XY37718 (Under Opal Labs)
DR-XY41630 (Under Opal Labs)

DATE OF FIRST AUTHORIZATION / RENEWAL OF AUTHORIZATION:
Initial: 14 May, 2003 (Under Getz Pharma)
Renewal: 22 April, 2008
Initial: 30 March, 2010 (Under Opal Labs)
Initial: 29 January, 2013 (Under Opal Labs)
Renewal: 22 March, 2018 (Under Opal Labs)

DATE OF REVISION OF PACKAGING INSERT
09 May, 2018.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Getz pharma (PVT) LIMITED
www.getzpharma.com
A member of The Getz Group, USA.

PH-200009760

Manufactured by: Opal Laboratories (Pvt.) Ltd., LC-41, L.I.T.E., Landhi, Karachi, Pakistan.
For: Getz Pharma (Pvt.) Ltd., 29-30/27, K.I.A., Karachi - 74900, Pakistan.
Imported by: Getz Pharma (Phils.) Inc., 2/F Tower 1, The Rockwell Business Center, Ortigas Ave., Pasig City, Philippines.