For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

UNILAX ORAL SOLUTION

1. Generic Name

Lactulose Solution U.S.P.

2. Qualitative and quantitative Composition:

Composition:

Each 15 ml contains:

Lactulose Concentrate I.P.

eq. to Lactulose 66%……...….10 g

Flavoured Syrupy base…….q.s.

The excipients used are Sorbitol, Sodium Benzoate, Bronopol, Citric Acid Monohydrate, Purified Water.

3. Dosage form and strength

Dosage form: Oral Solution

Strength: 10 gm

4. Clinical particulars

4.1. Therapeutic indication

(1) For the treatment of constipation
(2) Intestine preparation before any surgery
(3) For the treatment of hepatic encephalopathy

4.2. Posology and method of administration

Constipation:

The lactulose solution may be administered diluted or undiluted. Each dose may if necessary be taken with water or fruit juices, etc.

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

For lactulose 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 lactulose 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.

Lactulose oral solution

	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

* If the maintenance dose is below 15 ml, lactulose in bottles should be used. For a precise dosing for infants and children up to 7 years lactulose in bottles should be used.

Dosing in HE (for adults only):

Starting dose: 3 to 4 times daily 30-45 ml (6-9 x 5 ml spoonfuls). This dose may be adjusted to the maintenance dose to achieve two or three soft stools each day.

Paediatric population

The safety and efficacy in children (newborn to 18 years of age) with HE has 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.

4.3. Contraindications

- Hypersensitivity to any of the components of the product.
- Use in patients with galactosaemia. (Patients who require a low galactose diet)
- Acute inflammatory bowel disease (ulcerative colitis, Crohn's disease),
- gastrointestinal obstruction or subocclusive syndromes, digestive perforation or risk
- of digestive perforation, painful abdominal syndromes of undetermined cause.

4.4. Special warnings and precautions for use

In case of insufficient therapeutic effect after several days consultation of a physician is advised.

Patients with rare hereditary problems of galactose or fructose intolerance, lactase deficiency or glucose-galactose mal-absorption should not take this medicine.

Lactulose should be administered with care to patients who are intolerant to lactose.

The dose normally used should not pose a problem for diabetics.

For patients with gastro-cardiac syndrome (Roemheld syndrome) lactulose should only be taken after consultation of a physician. If symptoms like meteorism or bloating occur in such patients after lactulose intake, the dose should be reduced or the treatment should be discontinued.

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

For elderly patients or patients that are in bad general condition and who take lactulose for a more than 6 months period, periodic control of electrolytes is indicated.

During the therapy with laxatives, it is recommended to drink sufficient amounts of fluids (1.5-2 l/day, equal to 6-8 glasses).

Children

Use of laxatives in children should be exceptional and under medical supervision. Lactulose should be administrated with caution in infants and small children with autosomal recessive hereditary fructose intolerance.

The defecation reflex may be altered during the treatment with lactulose.

4.5. Drugs interactions

Lactulose may increase the loss of potassium induced by other drugs (e.g. thiazides, steroids and amphothericin B). Concomitant use of cardiac glycosides can increase the effect of the glycosides through potassium deficiency.

With increasing dosage, a decrease of pH-value in the colon is found. Therefore, drugs which are released in the colon pH-dependently (e.g. 5-ASA) can be inactivated.

4.6. Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

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

Lactulose can be used during pregnancy.

Lactation

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

Lactulose can be used during breast-feeding.

Fertility

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

4.7. Effects on ability to drive and use machines.

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

4.8. Undesirable effects

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

If high doses (normally only associated with portosystemic encephalopathy, PSE) are used for an extended period of time, the patient may experience an electrolyte imbalance due to diarrhoea. Dosage should then be adjusted to obtain two or three formed stools per day.

Gastrointestinal disorders

Flatulence, abdominal pain, nausea and vomiting. If dosed too high, diarrhoea.

Investigations

Electrolyte imbalance due to diarrhoea.

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	≥ 1/10
Common	≥1/100 to < 1/10
Uncommon	≥1/1,000 to <1/100
Rare	≥1/10,000 to < 1/1,000
Very rare	< 1/10,000

Not known	cannot be estimated from the available data

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 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. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com or at email: pv@torrentpharma.com or call on 1800-120-3001.

4.9. Overdose

If the dose is too high, the following may occur:

Symptom: diarrhoea and abdominal pain.

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

No specific antidote. Symptomatic treatment should be given.

5. Pharmacological properties

5.1. Mechanism of Action

Lactulose is a synthetic disaccharide derivative of lactose that consists of one molecule of galactose and one molecule of fructose. Saccharolytic bacteria present in the large intestine subsequently break the substance down into organic acids like lactic acid and small amounts of formic and acetic acids. Such resultant volatile fatty acid metabolites, in combination with hydrogen and methane that is also generated consequently enhance intraluminal gas formation, peristaltic gut motility, and elicit an osmotic effect that facilitates an increase in the water content of stool as well as associated stool softening. All of these actions ultimately assist in facilitating and increasing the frequency of bowel movements in patients experiencing constipation, although it may take 24 to 48 hours after using the medication for this laxative effect to become evident.

At the same time, the formation of such acids via the metabolism of lactulose by colonic bacteria also acidifies the contents of the colon, thereby contributing to the treatment of portal-systemic encephalopathy (PSE). As one of the principal features of PSE involves the accumulation of nitrogenous waste products like ammonia in the systemic circulation, a state in which the colonic contents become more acidic than blood allows ammonia in the

circulation to diffuse into the colon. Furthermore, ammonia that diffuses into the acidic colon is ionized to ammonium ions that are incapable of being absorbed back into the blood. These effects, combined with the laxative action of lactulose facilitates the excretion of excess ammonia. And finally, it is also believed that an acidic colonic environment results in the elimination of urease-producing bacteria that contribute to the formation of ammonia while surviving colonic bacteria use up any trapped ammonia in the colon as a source of nitrogen for protein synthesis.

5.2. Pharmacokinetic properties

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 colonic contents. These effects stimulate peristalsis of the colon and return the consistency of the stool. The constipation is cleared, 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 the bacterial nitrogen metabolism by stimulating the bacteria to utilize ammonia for bacterial protein synthesis.

5.3. 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 dosages, a proportion may be excreted unchanged.

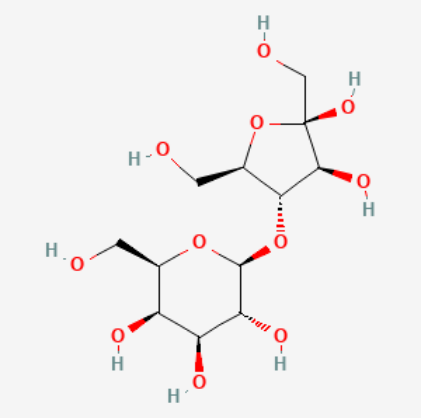
6. Nonclinical properties

6.1. Animal Toxicology or Pharmacology

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 the gastrointestinal tract than to a more specific toxic activity. In reproduction and teratology experiments in rabbits, rats or mice no adverse effects were found.

7. Description

Lactulose is (2S,3R,4S,5R,6R)-2-[(2R,3S,4S,5R)-4,5-dihydroxy-2,5-bis(hydroxymethyl) oxolan-3-yl]oxy-6-(hydroxymethyl) oxane-3,4,5-triol. The empiric formula of $C_{12}H_{22}O_{11}$ and its molecular weight is 342.30 g/mol. Its structural formula is:



UNILAX ORAL SOLUTION is a clear colourless to tight amber coloured liquid filled in milky PET bottles. The excipients used are Sorbitol, Sodium Benzoate, Bronopol, Citric Acid Monohydrate, Purified Water.

8. Pharmaceutical particulars

8.1. Incompatibilities

Not applicable

8.2. Shelf-life

Do not use later than date of expiry.

8.3. Packaging information

UNILAX ORAL SOLUTION is available in 100ml, 200ml & 450 ml in Bottle pack.

8.4. Storage and handing instructions.

Store below 30°C. Do not freeze.

Shake well before use.

Keep tightly closed after every use.

Keep out of reach of children.

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies.
- Have kidney or liver problems.
- Are pregnant or plan to become pregnant.
- Are breastfeeding or plan to breastfeed.
- Have any serious illness.
- Are taking any medicines (prescription, over the counter, vitamins, or herbal products)

10. Details of manufacturer

Manufactured by:

Prosperity Drugs Pvt. Ltd.

Village-Belikhol, Baddi-

Nalagarh Road, Distt. Solan- 174101 (H.P.).

11. Details of permission or licence number with date

Mfg Lic No. MNB/05/200 issued on 25.04.2024.

12. Date of revision

NA

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

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