PRODUCT MONOGRAPH

LIVOLUK SOLUTION

Each 15 ml contains:

Lactulose 10 g (As Lactulose concentrate USP)

Constipation- Osmotic Laxative Agent

Manufactured By:

Panacea Biotec Limited.

(Address as on Package)

Date of Preparation:

(24-07-2019)

Livoluk Solution

Each 15 ml contains:

Lactulose 10 g (As Lactulose concentrate USP)

Constipation- Osmotic Laxative Agent

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	**Dosage Form / Strength**	**Approved Indications**
Oral	Solution Each 15 ml contains: Lactulose 10 g (As Lactulose concentrate USP	Livoluk solution is an osmotic laxative drug indicated for: - Constipation

INDICATIONS AND CLINICAL USE:

Livoluk solution is indicated for :

Treatment of constipation,chronic constipation, after haemorrhoidectomy, in elderly after Barium meal examination, in bed ridden or institutionalized patients and others.

Prevention and treatment of portal systemic encephalopathy including the stages of hepatic pre-coma and coma. Livoluk reduces blood ammonia levels by 25% to 50%. This generally parallels improved mental state and EEG patterns.

Clinical Use in special population:

Pregnancy :

Reproduction studies have been performed in mice, rats, and rabbits at doses up to 2 or 4 times the usual human oral dose and have revealed no evidence of impaired fertility or harm to the fetus due to lactulose. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Lactation:

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.

Children :

Very little information on the use of lactulose in pediatric patients has been recorded.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

There are no known human data on long-term potential for carcinogenicity, mutagenicity, or impairment of fertility.

There are no known animal data on long-term potential for mutagenicity.

Administration of lactulose solution in the diet of mice for 18 months in concentrations of 3 and 10 percent (v/w) did not produce any evidence of carcinogenicity.

In studies in mice, rats, and rabbits, doses of lactulose solution up to 6 or 12 mL/kg/day produced no deleterious effects on breeding, conception, or parturition.

CONTRAINDICATIONS:

Since lactulose solution contains galactose (less than 1.6 g/15 mL), it is contraindicated in patients who require a low **galactose diet**.

WARNING AND PRECAUTIONS:

Electro-Cautery Procedures :

A theoretical hazard of explosion due to accumulation of H_2 gas may exist for patients being treated with lactulose who may undergo electrocautery procedures during proctoscopy or colonoscopy. Hence, patients should have a thorough bowel cleansing with a nonfermentable solution before pursuing the procedure.

Diabetics:

Lactulose solution contains galactose (<2.2 g/15 ml) and lactose(<1.2 g/15 ml). Use with caution in these individuals.

Concomitant laxative use:

Do not use other laxatives, especially during the initial phase of therapy for Portal Systemic Encephalopathy; the resulting loose stools may falsely suggest adequate lactulose dosage.

Monitoring:

In Portal Systemic Encephalopathy, electrolyte disturbances may require intensive monitoring and another specific therapy

Pregnancy: Teratogenic Effects : Category B

ADVERSE EFFECTS :

Gaseous distention with flatulence or belching and abdominal discomfort, such as cramping may occur.

Excessive dosage can lead to diarrhoea, nausea and vomiting.

DRUG INTERACTIONS :

Neomycin and other anti-infective agents may eliminate certain colonic bacteria and may interfere with the desired degradation of lactulose and prevent the acidification of colonic contents. Monitor the patient if concomitant oral infectives are given

Antacids:

Nonabsorbable antacids given concurrently with lactulose may inhibit the desired lactulose-induced drop in colonic pH.

DOSAGE AND ADMINISTRATION:

Treatment of Constipation :

Adults 15 to 30 ml daily, increased to 60 ml/day, if necessary.

Children :

Recommended initial daily dose in infants is 2.5ml twice daily. Children aged between 1 - 5 years can be given 5 ml twice daily. For older children and adolescents, the initial dose of 10ml twice daily can be administered. The total daily dose is 40 to 90 ml. If the initial dose causes diarrhoea, reduce immediately. If diarrhoea persists, discontinue use.

Prevention and treatment of portal-systemic encephalopathy :

Adults :

30 to 45 ml,3 or 4 times daily to produce 2 or 3 soft stools daily. Hourly doses of 30 to 45 ml may be used to induce rapid laxation in the initial phase of the therapy. When the laxative effect has been achieved, reduce dosage to recommended daily dose. Improvement may occur within 24 hours, but may not begin before 48 hours or later. Continuous long-term therapy is indicated to lessen severity and prevent recurrence of portal systemic encephalopathy.

Children : No dosage recommendations for this indication.

OVERDOSE

There have been no reports of accidental overdosage. It is expected that diarrhoea and abdominal cramps would be the major symptoms. Discontinue the medication.

ACTION AND CLINICAL PHARMACOLOGY:

PHARMACOLOGY

Lactulose,a synthetic disaccharide analog of lactose containing galactose and fructose, decreases blood ammonia concentrations and reduces the degree of portal systemic encephalopathy.

PHARMACOKINETICS

Lactulose is poorly absorbed. When given orally, only small amounts reach the blood. Urinary excretion is less than or equal to 3% and is essentially complete within 24 hours. Lactulose exerts its effect only in the colon. Transit time through the colon may be slow, therefore, 24-48 hours may be required to produce a normal bowel movement.

PHARMACODYNAMICS :

The human gastrointestinal tissue does not have any enzyme capable of hydrolysis of this disaccharide; as a result oral dose passes to the colon virtually unchanged. After reaching the colon, lactulose is metabolized by bacteria (*Lactobacillus, Bacteroides, Escherichia coli and Streptococcus faecalis*) resulting in the formation of low molecular weight acids (lactic acid, formic acid, acetic acid) and

carbon dioxide. These products produce an increased osmotic pressure and slightly acidify the colonic contents, resulting in an increase in stool water content and stool softening. Since the colonic contents are more acidic than the blood, ammonia can migrate from the blood into the colon. The acid colonic contents convert Ammonia (NH_3) to the ammonium ion $[NH_4]^+$, trapping it and preventing its absorption. The laxative action of the lactulose metabolites then expels the trapped ammonium ion $[NH_4]^+$ from the colon. Lactulose may also interfere with glutamine dependent non-bacterial ammonia production in the intestinal wall.

STORAGE AND HANDLING:

Preserve in tight container, preferably at a temperature between 2°C and 30°C. Avoid subfreezing temperatures

DOSAGE FORM– Solution

COMPOSITION - Each 15 ml contains :

Lactulose 10 g (As Lactulose concentrate USP)

PACKAGING – 100 ml

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

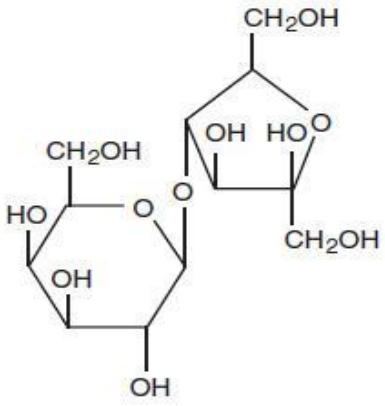
Drug Substance

Common Name: Lactulose

Chemical Name:

4-0-β-D-galactopyranosyl-D-fructofuranose

Lactulose has the following chemical structure :



The molecular weight is 342.30 g/mol. The molecular formula is C12H22011

REFERENCES :

1. Oilin BR. Lactulose. Drugs Facts and Comparisons, St Louis: Wolters Kluwar Company, 1995;49th Ed.:1833-1834.

2. Clausen MR and Mortensen PB. Lactulose, Disaccharides and Colonic flora. Clinical Consequences. Drugs 1997; 53(6):930-942.

3. Muller M and Jaquenoud E. Treatment of constipation in pregnant women. A multicenter study in a gynecological practice. Schweiz Med Wochenschr. 1995;125(36):1689-93

4. Romanczuk W and Korczowski R. Duphalac (lactulose) in the treatment of chronic constipation children. Wiad Lek. 1995;48(1-12):96-9

5. Dot TV and Petit - Young NA. Lactulose in the management of constipation : A Current Review. The Annals of Pharmacotherapy, 1992; 26: 1277-1281

6. Lactulose. In Martindale, the complete drug reference, edited by Sean C. Sweetman. Pharmaceutical Press 2002. 33rd edition: Pg. 1230

PART III: PATIENT INFORMATION

Livoluk Solution

This leaflet is a summary and will not tell you everything about the combination. Contact your doctor or pharmacist if you have any questions about the drug

Generic Name: Lactulose (Pronunciation : LAK-tyoo-lose)

- What is lactulose (Lactulose Solution)?
- What are the possible side effects of lactulose (Lactulose Solution)?
- What is the most important information I should know about lactulose (Lactulose Solution)?
- What should I discuss with my healthcare provider before taking lactulose (Lactulose Solution)?
- How should I take lactulose (Lactulose Solution)?
- What happens if I miss a dose (Lactulose Solution)?
- What happens if I overdose (Lactulose Solution)?
- What should I avoid while taking lactulose (Lactulose Solution)?
- What other drugs will affect lactulose (Lactulose Solution)?
- Where can I get more information?

What is lactulose (Lactulose Solution)?

Lactulose is a type of sugar. It is broken down in the large intestine into mild acids that draw water into the **colon**, which helps soften the stools.

Lactulose is used to treat chronic constipation.

Lactulose may also be used for other purposes not listed in this medication guide.

What are the possible side effects of lactulose (Lactulose Solution)?

Get **emergency medical help** if you have any of these **signs of an allergic reaction:** hives; difficulty breathing; swelling of your face, lips, tongue, or throat.

Stop using lactulose and call your doctor at once if you have severe or ongoing diarrhea.

Less serious side effects may include:

- bloating, gas;
- stomach pain;
- diarrhea; or
- nausea, vomiting.

This is not a complete list of side effects and others may occur. Tell your doctor about any unusual or bothersome side effect. You may report side effects to FDA at 1-800-FDA-1088.

Read the Lactulose Solution (lactulose solution) Side Effects Center for a complete guide to possible side effects

What is the most important information I should know about lactulose (Lactulose Solution)?

You should not use this medication if you are on a special **diet** low in galactose (milk sugar).

Before taking lactulose, tell your doctor if you have diabetes or if you need to have any type of intestinal test using a scope (such as a colonoscopy).

It may take up to 48 hours before you have a bowel movement after taking lactulose.

Stop using lactulose and call your doctor at once if you have severe or ongoing diarrhea.

The liquid form of lactulose may become slightly darken in color, but this is a harmless effect. However, do not use the medicine if it becomes very dark, or if it gets thicker or thinner in texture.

If you use lactulose over a long period of time, your doctor may want you to have occasional blood tests. Do not miss any scheduled appointments.

What should I discuss with my healthcare provider before taking lactulose (Lactulose Solution)?

You should not use this medication if you are on a special **diet** low in galactose (milk sugar).

Before taking lactulose, tell your doctor if you have:

- diabetes; or
- if you need to have any type of intestinal test using a scope (such as a **colonoscopy**).

If you have any of these conditions, you may need a dose adjustment or special tests to safely take lactulose.

FDA pregnancy category B. This medication is not expected to be harmful to an unborn baby. Tell your doctor if you are pregnant or plan to become pregnant during treatment.

It is not known whether lactulose passes into breast milk or if it could harm a nursing baby. Do not use this medication without telling your doctor if you are breast-**feeding a baby**.

How should I take lactulose (Lactulose Solution)?

Take this medication exactly as prescribed by your doctor. Do not take it in larger amounts or for longer than recommended. Follow the directions on your prescription label.

Measure liquid medicine with a special dose-measuring spoon or cup, not a regular table spoon. If you do not have a dose-measuring device, **ask** your pharmacist for one.

The liquid form of lactulose may become slightly darken in color, but this is a harmless effect. However, do not use the medicine if it becomes very dark, or if it gets thicker or thinner in texture.

Lactulose powder should be mixed with at least 4 ounces of water. You may also use fruit juice or milk to make the medication better.

It may take up to 48 hours before you have a bowel movement after taking lactulose.

If you use lactulose over a long period of time, your doctor may want you to have occasional blood tests. Do not miss any scheduled appointments.

Store lactulose at room temperature away from moisture and heat.

What happens if I miss a dose (Lactulose Solution)?

Take the missed dose as soon as you remember. If it is almost time for your next dose, wait until then to take the medicine and skip the missed dose. **Do not** take extra medicine to make up the missed dose.

What happens if I overdose (Lactulose Solution)?

Seek emergency medical attention if you think you have used too much of this medicine.

Overdose symptoms may include diarrhea, stomach pain, hot and dry skin, confusion, uneven heart rate, extreme thirst, increased urination, leg discomfort, and muscle weakness or limp feeling.

What should I avoid while taking lactulose (Lactulose Solution)?

Avoid using antacids without your doctor's advice. Use only the specific type of antacid your doctor recommends. Antacids contain different medicines and some types can make it harder for your body to absorb lactulose.

What other drugs will affect lactulose (Lactulose Solution)?

There may be other **drugs** that can interact with lactulose. Tell your doctor about all your prescription and over-the-counter medications, vitamins, minerals, herbal products, and drugs prescribed by other **doctors**. Do not start a new medication without telling your doctor.

Where can I get more information?

Your pharmacist can provide **more** information about lactulose.