SUMMARY OF PRODUCT CHARACTERISTICS

LIVOLUK
(Lactulose solution USP)

1. NAME OF THE MEDICINAL PRODUCT

Livoluk (Lactulose Solution USP)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 15 ml contains:
Lactulose …….10 g
(As Lactulose concentrate USP)
Palatable base q.s

3. PHARMACEUTICAL FORM

Solution for oral administration

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

(1) For the treatment of constipation
(2) For the treatment of hepatic encephalopathy (portal systemic encephalopathy); hepatic coma.

4.2 Posology and Method of Administration:

Posology

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 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

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 Special 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 Interaction with Other Medicaments and Other Forms of Interaction

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 Pregnancy, Lactation and Fertility,

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.

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 Pharmacodynamic 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

5.2 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.

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 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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Purified water

6.2 Incompatibilities

None

6.3 Shelf Life

36 Months

6. 4 Storage Instructions

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

6.5 Nature and Contents of Container

Amber PET Bottle of 100 ml

6.6 Instructions for User Handling

Avoid subfreezing temperatures.
Keep the medicine out of reach of children.

7. Marketing Authorization Holder

Panacea Biotec Pharma Ltd.
B-1 Extn , A-27, MCIE, Mathura Road,
New Delhi – 110044, India

8. MARKETING AUTHORISATION NUMBER(S)

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9. DATE OF FIRST AUTHORISATION

Fresh Registration

10. DATE OF TEXT PREPARATION

Feb, 2020