PRESCRIBING INFORMATION

1. NAME OF THE MEDICINAL PRODUCT

Avilac Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Avilac aqueous oral solution contains 667 g lactulose per 1000 ml.

Lactulose oral solution contains residues from the route of production with known effect, see section 4.4.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution.

A clear, viscous liquid, colourless to brownish yellow.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

1. Constipation.

2. Acute and chronic hepatic encephalopathy

4.2 Posology and method of Administration

The lactulose solution may be administrated diluted or undiluted. The dose should be titrated according to the clinical response. Lactulose may be given as a single daily dose or in two divided doses, using the measuring cup.

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.

The measuring cup may be used.

Dosing in constipation or where a soft stool is considered of medical benefit

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.

	Avilac oral solution	
	Starting dose	Maintenance dose
Adults and adolescents	15 - 30 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

Dosing in acute and chronic hepatic encephalopathy (for adults only):

Starting dose: 3 times daily 30 –50 ml.
Maintenance dose: should be adjusted so that soft stools are produced 2 - 3 times per 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.

4.3 Contraindications

- Hypersensitivity to the active substance lactulose or to any of the excipients listed in section 6.1 .
- Galactosaemia
- Gastro-intestinal obstruction, digestive perforation or risk of digestive perforation.

4.4 Special warnings and precautions for use

Painful abdominal symptoms of undetermined cause should be evaluated to exclude undiagnosed perforation or obstruction or undiagnosed disease/condition that predisposes to either before the treatment is started.

In case of insufficient therapeutic effect after several days the dose and/or additional measures should be re-considered.

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

It should be taken into account that the defecation reflex could be disturbed during the treatment.

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

The dose used in the treatment of HE is usually much higher and may need to be taken into consideration for diabetics.

Information on residues from manufacturing with known effect:

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

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

This product contains sulphite from the route of production.

Paediatric population

Use of laxatives in children should be exceptional and under medical supervision.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Avilac oral solution can be used during pregnancy.

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

Avilac 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
Avilac 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. See also overdose section 4.9.

If high doses (normally only associated with hepatic encephalopathy, HE) 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.

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 (frequency cannot be estimated from the available data)

MedDRA SOC	Frequency category			
	Very common	Common	Uncommon	Not known
Gastrointestinal disorders	Diarrhoea	Flatulence, abdominal pain, nausea, vomiting		
Investigations			Electrolyte imbalance due to diarrhoea	
Immune system disorders				Hypersensitvity reactions
Skin and subcutaneous tissue disorders				Rash*, Pruritis*, urticaria*

*Post-marketing experience

Paediatric population

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

Reporting of suspected 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.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

Additionally, you can also report to: Padagis.com.

4.9 Overdose

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

Symptom: diarrhoea, loss of electrolytes 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. Sympatomatic treatment should be given.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Osmotically acting laxatives ,ATC code: A 06A D11

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
None

6.2 Incompatibilities
Not known.

6.3 Shelf life
The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store in a cool place, below 25°C.

6.5 Nature and contents of container

HDPE white or PET amber round 300ml bottles plastic chilled resistance screw cap. The product is marketed with a plastic measuring cup.

7. MANUFACTURER

Padagis Israel Pharmaceuticals Ltd., 1 Rakefet st. Shoham

8. REGISTRATION HOLDER

Padagis Israel Pharmaceuticals Ltd., 1 Rakefet st. Shoham

9. REGISTRATION NUMBER

031-75-25187-00

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