SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
LAXAMOT 667 mg/ml Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
The solution of 1000 ml contains;

Active substance(s):
Lactulose (derived from cow milk) 667 g

Excipients:
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Oral solution.
Clear, colorless or pale brown-yellow viscous solution

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
- Constipation: Ensure that the colon acquires normal physiological rhythm
- In cases where the stool consistency is medically desired to be soft (after surgical procedures for hemorrhoids, colon or anus)
- Hepatic encephalopathy (HE): Used in the treatment and prophylaxis of hepatic coma or precoma.

4.2. Posology and method of administration
Posology/Frequency of administration and duration of the treatment:
The lactulose solution may be administered diluted or undiluted. If necessary, dose may be taken with water, fruit juices, milk etc.

Each dose of lactulose should be swallowed in one and should not be kept in the mouth for an extended period of time, because the sugar content can cause tooth decay when LAXAMOT is used for long periods of time

The posology should be adjusted according to the individual needs of the patient.

When a single daily dose is prescribed, the dose should be taken regularly and at the same time of day (e.g. during breakfast). During the therapy with laxatives it is recommended to drink sufficient amounts of fluids (1.5–2 liters, equal to 6-8 glasses) during the day.

For lactulose in bottles the measuring cup may be used.

<u>Dosing in constipation or in cases where the stool consistency is medically desired to be soft</u>
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 in bottles:

	Starting dose daily	**Maintenance dose daily**
Adults and adolescents	15 – 45 ml *(10-30 g)*	15 – 30 ml *(10-20 g)*
Children (7-14 years)	15 ml *(10 g)*	10- 15 ml *(7-10 g)*
Children (1-6 years)	5 – 10 ml *(3-7 g)*	5 – 10 ml *(3-7 g)*
Infants under 1 year	up to 5 ml *(up to 3 g)*	up to 5 ml *(up to 3 g)*

Dosing in HE (hepatic encephalopathy) (for adults only):
Initial dose: 3 to 4 times daily 30-45 ml *(20-30 g)*
This dose may be adjusted to the maintenance dose to achieve two or three soft stools each day.

Method of administration:
For oral use.

Additional information for special populations:
Renal/Hepatic Failure:
No special dosage recommendations are available, since systemic exposure to lactulose is negligible.

Pediatric population:
Information on the dose of use in children of different age groups is given in the table above.

The safety and efficacy in children (newborn to 18 years of age) with HE (hepatic encephalopathy) have not been established.
No data are available.

Geriatric population:
No special dosage recommendations are available, since systemic exposure to lactulose is negligible.

4.3. Contraindications
- Hypersensitivity to the active substance or any of the excipients
- Galactosaemia
- Gastro-intestinal obstruction, digestive perforation or risk of digestive perforation

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

4.4. Special warnings and precautions for use
Consultation of a physician is advised in case of:
- Painful abdominal symptoms of undetermined cause before the treatment is started
- Insufficient therapeutic effect after several days

Lactulose should be administered with care to patients who are intolerant to lactose (see section 6.1 'List of excipients'). 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.

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

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

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

4.5. Interactions with other medicinal products and other forms of interactions
Interaction studies have not been conducted.

Additional information for special populations:
Not known.

4.6. Fertility, pregnancy and lactation
General advise
Pregnancy category B.

Women of childbearing potential / Birth control (Contraception)
There is no specific recommendation regarding the use of LAXAMOT in women of childbearing potential, or there is no information on whether birth control is necessary during or after treatment.

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

LAXAMOT 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.

LAXAMOT can be used during breast-feeding.

Reproduction/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 diarrhea 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 diarrhea. Dosage should then be adjusted to obtain two or three defecation per day.

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 based on available data).

According to the MedDRA system organ class:

Gastrointestinal disorders
Very common: Diarrhea
Common: Flatulence, abdominal pain, nausea, vomiting

Investigations
Uncommon: Electrolyte imbalance due to diarrhea

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

4.9. Overdose and treatment
If the dose is too high, the following may occur:
Symptom: diarrhea and abdominal pain
Treatment: cessation of treatment or dose reduction. Extensive fluid loss by diarrhea or vomiting may require correction of electrolyte disturbances.

No specific antidote. Symptomatic treatment should be given.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Osmotically acting laxatives
ATC code: A06AD11

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 a regular defecation is provided. 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 such as lactobacillus, trapping of ammonia in the ionic form in colon by acidification of the colonic contents, catharsis due to the low pH in the colon as well as an osmotic effect, alteration of the bacterial nitrogen metabolism by stimulating the bacteria to utilize ammonia during bacterial protein synthesis.

While lactulose promotes the proliferation of beneficial bacteria such as Bifidobacterium and Lactobacillus as a prebiotic substance, it can suppress bacterial pathogenic potencies such as *Clostridium* and *Escherichia coli*. This can lead to a more positive balance in the intestinal flora.

5.2. Pharmacokinetic properties

Absorption / Distribution:

Lactulose is poorly absorbed after oral administration.

Metabolism:

Since it is absorbed in very small amount, lactulose reaches the colon almost unchanged and there it is metabolized by the bacteria. Metabolism is complete at doses up to 25-50 g or 40-75 ml.

Excretion:

When applied at doses above 25-50 g or 40-75 ml, a proportion may be excreted unchanged through feces.

5.3. Preclinical safety data

The results of acute, sub-chronic and chronic toxicity studies in various experimental animals indicate that the product has very low toxicity. The effects observed, appear to be more related to the effect of solid feces 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

It does not contain any excipients, but it may contain small amounts of the relevant sugars (e.g. lactose, galactose, epilactose, fructose) that occur during synthesis.

6.2. Incompatibilities

There is no known incompatibility.

6.3. Shelf life

24 months (if stored in undamaged original packaging).
It can be used during shelf life after product is opened.

6.4. Special precautions for storage

It should be stored at room temperature below 25 ° C.
It should be kept in its undamaged original packaging.

6.5. Nature and contents of container

It is presented in a 300 ml high density polyethylene (HDPE) bottle closed with polyethylene (PE) cap packaged together with 30 ml polypropylene (PP) measuring cup.

6.6. Special precautions for disposal and other handling

There are no special precautions.

7. MARKETING AUTHORIZATION HOLDER

Berko İlaç ve Kimya San. A.Ş.
Yenişehir Mah. Özgür Sok. No: 16-18 Ataşehir/İstanbul-Türkiye
+90 216 456 65 70 (Pbx)
+90 216 456 65 79 (Fax)
info@berko.com.tr

8. MARKETING AUTHORIZATION NUMBER(S)

2019/676

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION

Date of the first authorization: 18.12.2019
Date of the renewal of the authorization:

10. DATE OF REVISION OF THE TEXT

04.02.2021