

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Laxatev 13.8g Powder for Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains the following active ingredients:

Macrogol 3350	13.125 g
Sodium chloride	0.3507 g
Sodium hydrogen carbonate	0.1785 g
Potassium chloride	0.0466 g

The content of electrolyte ions per sachet when made up to 125 ml of solution is as follows:

Sodium	65 mmol/l
Chloride	53 mmol/l
Hydrogen carbonate	17 mmol/l
Potassium	5 mmol/l

Excipient with known effect: sorbitol

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for Oral Solution

Single-dose sachet containing a free flowing white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the treatment of chronic constipation.

For the treatment of faecal impaction, defined as refractory constipation with faecal loading of the rectum and/or colon.

4.2 Posology and method of administration

Posology:

Chronic constipation

A course of treatment for constipation with Laxatev 13.8 g does not normally exceed 2 weeks, although this can be repeated if required.

As for all laxatives, prolonged use is not usually recommended. Extended use may be necessary in the care of patients with severe chronic or resistant constipation, secondary to multiple sclerosis or Parkinson's Disease, or induced by regular constipating medication in particular opioids and antimuscarinics.

Adults, adolescents and the elderly: 1-3 sachets daily in divided doses, according to individual response. For extended use, the dose can be adjusted down to 1 or 2 sachets daily.

Children (below 12 years of age): Not recommended. Alternative products are available for children.

Patients with renal insufficiency: No dosage change is necessary.

Faecal impaction

A course of treatment for faecal impaction with Laxatev 13.8 g does not normally exceed 3 days.

Adults, adolescents and the elderly: 8 sachets daily, all of which should be consumed within a 6 hour period.

Children (below 12 years of age): Not recommended. Alternative products are available for children.

Patients with impaired cardiovascular function: For the treatment of faecal impaction the dose should be divided so that no more than two sachets are taken in any one hour.

Patients with renal insufficiency: No dosage change is necessary.

Method of administration:

Each sachet should be dissolved in 125 ml water. For use in faecal impaction 8 sachets may be dissolved in 1 litre of water.

4.3 Contraindications

Intestinal perforation or obstruction due to structural or functional disorder of the gut wall, ileus, severe inflammatory conditions of the intestinal tract, such as Crohn's disease and ulcerative colitis and toxic megacolon.

Hypersensitivity to the active substances or any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

The fluid content of *Laxatev 13.8 g* when re-constituted with water does not replace regular fluid intake and adequate fluid intake must be maintained.

Diagnosis of faecal impaction/faecal loading of the rectum should be confirmed by physical or radiological examination of the abdomen and rectum.

Mild adverse drug reactions are possible as indicated in section 4.8. If patients develop any symptoms indicating shifts of fluids/electrolytes (e.g. oedema, shortness of breath, increasing fatigue, dehydration, cardiac failure) *Laxatev 13.8 g* should be stopped immediately and electrolytes measured and any abnormality should be treated appropriately.

The absorption of other medicinal products could transiently be reduced due to an increase in gastro-intestinal transit rate induced by *Laxatev 13.8 g* (see section 4.5).

This medicine contains 0.63 mmol (25 mg) potassium per sachet. This should be taken into consideration by patients with reduced kidney function or patients on a controlled potassium diet.

This medicine contains 8.1 mmol (187 mg) sodium per sachet. This should be taken into consideration by patients on a controlled sodium diet.

The lemon lime flavour in *Laxatev 13.8 g* contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Macrogol 3350 raises the solubility of medicinal products that are soluble in alcohol and relatively insoluble in water. There is a possibility that the absorption of other medicinal products could be transiently reduced during use with *Laxatev 13.8 g* (see section 4.4).

There have been isolated reports of decreased efficacy with some concomitantly administered medicinal products, e.g.

anti-epileptics.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited amount of data from the use of macrogol 3350 in pregnant women. Studies in animals have shown indirect reproductive toxicity (see section 5.3). Clinically, no effects during pregnancy are anticipated, since systemic exposure to macrogol 3350 is negligible.

Laxatev 13.8 g can be used during pregnancy.

Breastfeeding

No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to macrogol 3350 is negligible.

Laxatev 13.8 g can be used during breast-feeding.

Fertility

There are no data on the effects of macrogol 3350 on fertility in humans. There were no effects on fertility in studies in male and female rats (see section 5.3).

4.7 Effects on ability to drive and use machines

Laxatev 13.8 g has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Reactions related to the gastrointestinal tract occur most commonly. These reactions may occur as a consequence of expansion of the contents of the gastrointestinal tract, and an increase in motility due to the pharmacologic effects of *Laxatev 13.8 g*. Mild diarrhoea usually responds to dose reduction.

The frequency of the adverse effects is not known as it cannot be estimated from the available data.

System Order Class	Adverse Events
Immune system disorders	Allergic reactions, including anaphylactic reactions, dyspnoea and skin reactions (see below)
Metabolism and nutrition disorders	Electrolyte disturbances, particularly hyperkalaemia and hypokalaemia
Nervous system disorders	Headache
Gastrointestinal disorders	Abdominal pain, diarrhoea, vomiting, nausea, dyspepsia, abdominal distension, borborygmi, flatulence, anorectal discomfort
Skin and subcutaneous tissue disorders	Allergic skin reactions, including angioedema, urticaria, pruritus, rash, erythema
General disorders and administration site conditions	Peripheral oedema

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. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Severe abdominal pain or distension can be treated by nasogastric aspiration. Extensive fluid loss by diarrhoea or vomiting may require correction of electrolyte disturbances.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Osmotically acting laxatives.

ATC code: A06A D65

Macrogol 3350 acts by virtue of its osmotic action in the gut, which induces a laxative effect. Macrogol 3350 increases the stool volume, which triggers colon motility via neuromuscular pathways. The physiological consequence is an improved propulsive colonic transportation of the softened stools and a facilitation of the defaecation. Electrolytes combined with macrogol 3350 are exchanged across the intestinal barrier (mucosa) with serum electrolytes and excreted in faecal water without net gain or loss of sodium, potassium and water.

For the indication of faecal impaction controlled comparative studies have not been performed with other treatments (e.g. enemas). In a non-comparative study in 27 adult patients, macrogol with electrolytes cleared the faecal impaction in 12/27 (44%) after 1 day's treatment; 23/27 (85%) after 2 days' treatment and 24/27 (89%) at the end of 3 days.

Clinical studies using macrogol with electrolytes for the treatment of chronic constipation have shown that the dose needed to produce normal formed stools tends to reduce over time. Many patients respond to between one and two sachets a day but this dose should be adjusted depending on individual response.

5.2 Pharmacokinetic properties

Macrogol 3350 is unchanged along the gut. It is virtually unabsorbed from the gastro-intestinal tract. Any macrogol 3350 that is absorbed is excreted via the urine.

5.3 Preclinical safety data

Preclinical studies provide evidence that macrogol 3350 has no significant systemic toxicity potential, based on conventional studies of pharmacology, repeated dose toxicity and genotoxicity.

There were no direct embryotoxic or teratogenic effects in rats even at maternally toxic levels that are a multiple of 66 x the maximum recommended dose in humans for chronic constipation and 25 x for faecal impaction. Indirect embryofetal effects, including reduction in fetal and placental weights, reduced fetal viability, increased limb and paw hyperflexion and abortions, were noted in the rabbit at a maternally toxic dose that was 3.3 x the maximum recommended dose in humans for treatment of chronic constipation and 1.3 x for faecal impaction. Rabbits are a sensitive animal test species to the effects of GI-acting substances and the studies were conducted under exaggerated conditions with high dose volumes administered, which are not clinically relevant. The findings may have been a consequence of an indirect effect of macrogol 3350 related to poor maternal condition as the result of an exaggerated pharmacodynamic response in the rabbit. There was no indication of a teratogenic effect.

There are long-term animal toxicity or carcinogenicity studies involving macrogol 3350. Results from these and other toxicity studies using high levels of orally administered high molecular weight macrogols provide evidence of safety at the recommended therapeutic dose.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Silica colloidal anhydrous
Saccharin sodium

Orange flavour

(Orange flavour contains: flavouring preparations and substances, natural flavouring substances, maltodextrin, acacia, α -tocopherol)

Lemon lime flavour

(Lemon lime flavour contains: natural lemon oil, natural powder flavour lemon, powder flavour lime, maltodextrin, mannitol, gluconolactone, sorbitol, acacia, silica colloidal anhydrous)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

Reconstituted solution: 24 hours

6.4 Special precautions for storage

Sachet: Do not store above 25°C.

Reconstituted solution: Store covered in a refrigerator (2°C to 8°C).

6.5 Nature and contents of container

The sachet is composed of paper, ethylene/methacrylic acid co-polymer and aluminium.

Sachets are packed in cartons of 20, 30 and 50.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Preparation of solution:

The content of each sachet should be dissolved in 125 ml water.

The solution is nearly colourless and slightly opalescent.

After 24 hours, any unused solution should be discarded.

7 MARKETING AUTHORISATION HOLDER

Teva Pharma B.V.
Swensweg 5
2031 GA Haarlem
The Netherlands

8 MARKETING AUTHORISATION NUMBER

PA0749/200/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28th February 2014

10 DATE OF REVISION OF THE TEXT

August 2017