Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Laxatev Paediatric 6.9g Powder for Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains the following active ingredients:

Macrogol 3350	6.563 g
Sodium chloride	175.4 mg
Sodium hydrogen carbonate	89.3 mg
Potassium chloride	23.3 mg

The content of electrolyte ions per sachet when made up to 62.5 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 in children 2 to 11 years of age.

For the treatment of faecal impaction in children 5 to 11 years of age, defined as refractory constipation with faecal loading of the rectum and/or colon.

4.2 Posology and method of administration

Posology:

Chronic constipation
The usual starting dose is 1 sachet daily for children aged 2 to 6 years and 2 sachets daily for children aged 7 to 11 years. The dose should be adjusted up or down as required to produce regular soft stools. If the dose needs to be increased this is best done every second day. The maximum dose needed does not normally exceed 4 sachets a day.

Treatment of children with chronic constipation needs to be for a prolonged period (at least 6 to 12 months). However, safety and efficacy have only been proved for a period of up to three months. Treatment should be stopped gradually and resumed if constipation recurs.

Faecal impaction
A course of treatment for faecal impaction is for up to 7 days as follows:

Daily dosage regimen:

Number of sachets							
Age (years)	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**
5 - 11	**4**	**6**	**8**	**10**	**12**	**12**	**12**

The daily number of sachets should be taken in divided doses, all consumed within a 12 hour period. The above dosage regimen should be stopped once disimpaction has occurred. An indicator of disimpaction is the passage of a large volume of stools. After disimpaction it is recommended that the child follows an appropriate bowel management program to prevent reimpaction (dosing for prevention of re-impaction should be as for patients with chronic constipation; see above).

Macrogol-ratiopharm 6.9 g is not recommended for children below five years of age for the treatment of faecal impaction, or in children below two years of age for the treatment of chronic constipation.

Patients with impaired cardiovascular function:
There are no clinical data for this group of patients. Therefore this medicinal product is not recommended for treating faecal impaction in children with impaired cardiovascular function.

Patients with renal insufficiency:
There are no clinical data for this group of patients. Therefore this medicinal product is not recommended for treating faecal impaction in children with impaired renal function.

Method of administration:
Each sachet should be dissolved in 62.5 ml (quarter of a glass) of water. The correct number of sachets may be reconstituted in advance and kept covered and refrigerated for up to 24 hours. For example, for use in faecal impaction, 12 sachets can be made up into 750 ml 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 Paediatric 6.9 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.

Rarely symptoms indicating shifts of fluid/electrolytes e.g. oedema, shortness of breath, increasing fatigue, dehydration and cardiac failure have been reported in adults when using preparations containing macrogol. If this occurs treatment should be stopped immediately, electrolytes measured, and any abnormality should be treated appropriately.

When used in high doses to treat faecal impaction this medicinal product should be administered with caution to patients with impaired gag reflex, reflux oesophagitis or diminished levels of consciousness.

The absorption of other medicinal products could transiently be reduced due to an increase in gastro-intestinal transit rate induced by *Laxatev Paediatric 6.9 g* (see section 4.5).

This medicine contains 0.3 mmol (12 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 4.1 mmol (94 mg) sodium per sachet. This should be taken into consideration by patients on a controlled sodium diet.

The lemon lime flavour in *Laxatev Paediatric 6.9 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

Medicinal products in solid dose form taken within one hour of administration of large volumes of macrogol preparations (as used when treating faecal impaction) may be flushed from the gastrointestinal tract and not absorbed.

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 Paediatric 6.9 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 Paediatric *6.9 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 Paediatric 6.9 mg 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 Paediatric *6.9 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 Paediatric 6.9 g*
In the treatment of chronic constipation, diarrhoea or loose stools normally respond to a reduction in dose.

Diarrhoea, abdominal distension, anorectal discomfort and mild vomiting are more often observed during the treatment

for faecal impaction. Vomiting may be resolved if the dose is reduced or delayed.

The frequency of the adverse reactions listed below is defined using the following convention: very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1000); and very rare (<1/10,000); not known (cannot be estimated from the available data).

System Order Class	Frequency	Adverse Events
Immune system disorders	Rare	Allergic reactions including anaphylactic reaction
	Not known	Dyspnoea and skin reaction (see below)
Metabolism and nutrition disorders	Not known	Electrolyte disturbances, particularly hyperkalaemia and hypokalaemia
Nervous system disorders	Not known	Headache
Gastrointestinal disorders	Very common	Abdominal pain, borborygmi
	Common	Diarrhoea, vomiting, nausea, anorectal discomfort
	Uncommon	Abdominal distension, flatulence
	Not known	Dyspepsia, peri-anal inflammation
Skin and subcutaneous tissue disorders	Not known	Allergic skin reactions including angioedema, urticaria, pruritus, rash, erythema
General disorders and administration site conditions	Not known	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.

In an open study of macrogol with electrolytes in chronic constipation, weekly defaecation frequency was increased from 1.3 at baseline to 6.7, 7.2 and 7.1 at weeks 2, 4 and 12 respectively. In a study comparing macrogol with electrolytes and lactulose as maintenance therapy after disimpaction, weekly stool frequency at the last visit was 9.4

(SD 4.46) in the macrogol with electrolytes group compared with 5.9 (SD 4.29). In the lactulose group 7 children re-impacted (23%) compared with no children in the macrogol with electrolytes group.

For the indication of faecal impaction comparative studies have not been performed with other treatments (e.g. enemas). In a non-comparative study in 63 children, macrogol with electrolytes (paediatric version) cleared the faecal impaction in the majority of patients within 3 - 7 days of treatment. For the 5 - 11 years age group the average total number of sachets of macrogol with electrolytes (paediatric version) required was 47.2.

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 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 62.5 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

PA0749/200/002

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