SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lacrofarm Junior, powder for oral solution, sachet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet of contains the following active ingredients:

Macrogol 3350	6.563g
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	5.4 mmol/l

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral solution.
Free flowing white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of chronic constipation in children 1 to 11 years of age.
For the treatment of faecal impaction in children from the age of 5 years, 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 1 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 increasing this is best done every second day. For children below 2 years of age, the maximum recommended dose should not exceed 2 sachets a day. For children aged 2 to 11 years, the maximum recommended 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 – 12 months). However, safety and efficacy of Lacrofarm Junior 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 with Lacrofarm Junior is for up to 7 days as follows:

Daily dosage regimen:

Number of Lacrofarm Junior 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).

Lacrofarm Junior is not recommended for children below 5 years of age for the treatment of faecal impaction, or in children below 1 year of age for the treatment of chronic constipation. For patients of 12 years and older it is recommended to use Lacrofarm.

Patients with impaired cardiovascular function: There are no clinical data for this group of patients. Therefore Lacrofarm Junior 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 Lacrofarm Junior 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 to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

The fluid content of Lacrofarm Junior 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 the 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, Lacrofarm Junior 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.

In patients with swallowing problems, who need the addition of a thickener to solutions to enhance an appropriate intake, interactions should be considered, see section 4.5.

When reconstituted the solution has no calorific value.

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

This medicinal product contains 93 mg (4.06 mmol) sodium per sachet, equivalent to 4.7% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

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 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 Lacrofarm Junior(see section 4.4). There have been isolated reports of decreased efficacy with some concomitantly administered medicinal products e.g. anti-epileptics. Therefore, other medicines should not be taken orally for one hour before, during and for one hour after taking Lacrofarm Junior.

Lacrofarm Junior may result in a potential interactive effect if used with starch-based food thickeners. The macrogol ingredient counteracts the thickening effect of starch, effectively liquefying preparations that need to remain thick for people with swallowing problems.

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.

Lacrofarm Junior 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 macrogol 3350 is negligible

Lacrofarm Junior 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

Lacrofarm Junior 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 Lacrofarm Junior.

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 Organ Class	Adverse event	Frequency
Immune system disorders	Allergic reactions including anaphylactic reactions	Rare
	Dyspnoea and skin reactions (see below)	Not known
Skin and subcutaneous tissue disorders	Allergic skin reactions including angioedema, urticaria, pruritus, rash, erythema	Not known
Metabolism and nutrition disorders	Electrolyte disturbances, particularly hyperkalaemia and hypokalaemia	Not known
Nervous system disorders	Headache	Not known
Gastrointestinal	Abdominal pain, borborygmi	Very common

disorders	Diarrhoea, vomiting, nausea and anorectal discomfort	Common
	Abdominal distension, flatulence	Uncommon
	Dyspepsia and peri-anal inflammation	Not known
General disorders and administration site conditions	Peripheral oedema	Not known

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 the national reporting system listed in Appendix V.

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.

In one retrospective-prospective study, 35 patients <24 months age were treated with macrogol with electrolytes for functional constipation for a mean duration of 4.6 ± 3.67 months (from 3 weeks to 18 months). Mean stool frequency before treatment was 2.34 ± 0.98 per week. Following treatment, the frequency of bowel movements was 7.31 ± 1.60 per week, which was a significant difference from baseline ($p < 0.001$). There was also a significant difference in improvement from baseline in the stool consistency score after treatment (1.57 ± 0.54 vs. 3.34 ± 0.58; $p < 0.001$).

In an observational, prospective, longitudinal, parallel group study 62 children aged 1-17 years were treated for chronic constipation with macrogol / macrogol with electrolytes for 12 weeks. Of these 62 patients 30 were aged 1–3 years. The number of bowel movements per week was similar in both groups at weeks 6 and 12: mean (SD) 6.1 (2.5) and 6.0 (2.7) at 6 weeks, and 4.6 (2.2) and 5.4 (1.8) at 12 weeks for macrogol and macrogol with electrolytes. Similar improved efficacy results were observed in 2 further trials where patients 6 months – 15 years were treated with macrogol with electrolytes.

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 and 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

Acesulfame potassium (E950)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years.

Reconstituted solution: 24 hours

6.4 Special precautions for storage
Reconstituted solution: Store at 2-8°C.

6.5 Nature and contents of container
Sachet: laminate consisting of four layers: low density polyethylene, aluminium, low density polyethylene and paper.

Pack sizes: Boxes of 2, 6, 8, 10, 20, 30, 40, 50, 60 or 100 sachets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
Any unused solution should be discarded within 24 hours.

7. MARKETING AUTHORISATION HOLDER
<To be completed nationally>

8. MARKETING AUTHORISATION NUMBER(S)
<To be completed nationally>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
<To be completed nationally>

10. DATE OF REVISION OF TEXT

2023-10-27