

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Compound Macrogol Vale 13.8 g Powder for Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains the following quantitative composition of active ingredients:

Macrogol 3350	13.125 g
Sodium Chloride	350.7 mg
Sodium Hydrogen Carbonate	178.5 mg
Potassium Chloride	46.6 mg

The content of electrolyte ions per sachet following reconstitution in 125 ml of water is equivalent to:

Sodium	65 mmol/l
Chloride	53 mmol/l
Bicarbonate	17 mmol/l
Potassium	5 mmol/l

Excipient with known effect:

Each sachet contains 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 crystalline powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of chronic constipation in adults and adolescents aged 12 years and over.

4.2 Posology and method of administration

Posology

A course of treatment for constipation with Compound Macrogol 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 old): Not recommended. Alternative macrogol products are available for children.

Method of administration

Compound Macrogol is for oral use.

Each sachet should be dissolved in 125 ml water.

4.3 Contraindications

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

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.

4.4 Special warnings and precautions for use

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), Compound Macrogol 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 macrogol 3350 (see section 4.5).

The lemon lime flavour in Compound Macrogol 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 macrogol 3350 (see section 4.4). There have been isolated reports of decreased efficacy with some concomitantly administered medicinal products, e.g. antiepileptics.

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.

Compound Macrogol can be used during pregnancy.

Breast-feeding

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

Compound Macrogol 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

Macrogol 3350 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 macrogol 3350. 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 Event
Immune system disorder	Allergic reactions, including anaphylaxis, angioedema, dyspnoea, rash, urticaria, and pruritus.
Skin and subcutaneous tissue disorders	Erythema
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 and anorectal discomfort.
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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Severe 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: A06AD65

Mechanism of action

Macroglol 3350 acts by virtue of its osmotic action in the gut, which induces a laxative effect. Macroglol 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 defecation. Electrolytes combined with macroglol 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.

Clinical efficacy and safety

Clinical studies in the use of macrogol 3350 in chronic constipation have shown that the dose needed to produce normal formed stools tends to reduce over time. Many patients respond to between 1 and 2 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 gastrointestinal 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 foetal 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

Silica, colloidal anhydrous

Saccharin sodium

Orange flavour

(Orange flavour contains: flavouring substances and flavouring preparations, maltodextrin, acacia gum, alpha-tocopherol)

Lemon lime flavour

(Lemon lime flavour contains: flavouring preparations, maltodextrin, mannitol, gluconolactone, sorbitol, acacia gum, 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 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 10, 20, 30 and 50.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

After 24 hours, any unused solution should be discarded.

7. MARKETING AUTHORISATION HOLDER

Generics [UK] Limited t/a Mylan
Station Close,
Potters Bar,
Hertfordshire, EN6 1TL

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 04569/1678

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

30/12/2015

10 DATE OF REVISION OF THE TEXT

20/10/2016