Australian Product Information - MOVIPREP® (macrogol 3350, sodium chloride, sodium sulfate, potassium chloride, ascorbic acid and sodium ascorbate) Powder for Oral Solution

1 NAME OF THE MEDICINE

Macrogol 3350, sodium chloride, sodium sulfate, potassium chloride, ascorbic acid and sodium ascorbate.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Sachet A:

Macrogol 3350	100 g
Sodium sulfate	7.5 g
Sodium chloride	2.691 g
Potassium chloride	1.015 g

Sachet B:

Ascorbic acid	4.7 g
Sodium ascorbate	5.9 g

The concentration of electrolyte ions when both sachets are made up to 1 litre of solution is:

Sodium	181.6 mmol/L (of which not more than 56.2 mmol is absorbable)
Sulfate	52.8 mmol/L
Chloride	59.8 mmol/L
Potassium	14.2 mmol/L
Ascorbate	56.5 mmol/L

Contains aspartame. Phenylketonurics are warned that this product contains aspartame (phenylalanine). See Section 4.3 Contraindications.

The complete treatment contains 8.4 g of sodium and 1.1 g of potassium. See Section 4.4 Special Warnings and Precautions for Use.

For a full list of excipients, see Section 6.1 List of Excipients.

3 PHARMACEUTICAL FORM

Powder for Oral Solution

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For bowel cleansing prior to any clinical procedure requiring a clean bowel, e.g., bowel endoscopy, lower gastrointestinal tract radiology or digestive tract surgery.

4.2 DOSE AND METHOD OF ADMINISTRATION

A course of treatment consists of two litres of MOVIPREP.

It is strongly recommended that patients also drink a further one litre of clear liquid to prevent them from feeling thirsty and becoming dehydrated. “Clear liquids” include:

- water,
- clear soup,
- tea or coffee without milk or non-dairy creamer,
- all of the following liquids which are not coloured red or purple: fruit juices without pulp, carbonated and non-carbonated soft drinks, fruit flavoured cordials.

Note: patients should not drink anything coloured red or purple.

A litre of MOVIPREP consists of one “Sachet A” and one “Sachet B” dissolved together in water to make a one litre solution. The reconstituted solution should be drunk over a period of one to two hours. This process should be repeated with a second litre of MOVIPREP to complete this course.

This course of treatment can be taken either as divided (split) or single doses and timing is dependent on whether the clinical procedures is conducted with or without general anaesthesia as specified below:

<u>For procedures conducted under general anaesthesia:</u>

1. Divided doses: one litre of MOVIPREP in the evening before and one litre of MOVIPREP in the early morning of the day of the procedure. Ensure consumption of MOVIPREP as well as any other clear fluids has finished at least two hour before the start of the clinical procedure

2. Single dose: two litres in the evening preceding the clinical procedure or two litres in the morning of the clinical procedure. Ensure consumption of MOVIPREP as well as any other clear fluids has finished at least two hour before the start of the clinical procedure.

<u>For procedures conducted without general anaesthesia:</u>

1. Divided doses: one litre of MOVIPREP in the evening before and one litre of MOVIPREP in the early morning of the day of the procedure. Ensure consumption of MOVIPREP as well as any other clear fluids has finished at least one hour before the start of the clinical procedure.

2. Single dose: two litres in the evening preceding the clinical procedure or two litres in the morning of the clinical procedure. Ensure consumption of MOVIPREP as well as any other clear fluids has finished at least one hour before the start of the clinical procedure.

Patients should be advised to allow for appropriate time to travel to the colonoscopy unit.

For patients taking the divided dose or the 2 litre dose taken the evening before the procedure, no solid food or liquids (other than the clear fluids listed above) should be taken from the start of the course of MOVIPREP treatment until after the clinical procedure.

For patients taking the 2 litre dose in the morning of the procedure, no solid food or liquids (other than the clear fluids listed above) should be taken from 6 pm the night before the procedure until after the clinical procedure.

Reconstitution of MOVIPREP in water may take up to 5 minutes and is best performed by adding the powder to the mixing vessel first followed by the water. The patient should wait until all the powder has dissolved before drinking the solution.

After reconstitution, the MOVIPREP solution may be used immediately or if preferred may be cooled before use. The reconstituted solution should be used within 24 hours.

4.3 CONTRAINDICATIONS

Intestinal perforation or obstruction due to structural or functional disorder of the gut wall, ileus, gastric retention, and severe inflammatory conditions of the intestinal tract, such as Crohn's disease, ulcerative colitis and toxic megacolon. Phenylketonuria (due to the presence of aspartame), glucose-6-phosphodehydrogenase deficiency (patients may be at risk of acute haemolysis due to the presence of ascorbate), known hypersensitivity to any of the active substances or to any of the excipients. Do not use in unconscious patients, or patients with severe dehydration.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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

Diarrhoea is an expected effect resulting from the use of MOVIPREP.

MOVIPREP should be administered with caution to frail or debilitated patients in poor health.

MOVIPREP should be used with caution in patients with:

- impaired gag reflex, with the possibility of regurgitation or aspiration, or with diminished levels of consciousness
- moderate or severe renal insufficiency (creatinine clearance <30 mL/min)
- cardiac failure (NYHA Grade III or IV)
- those at risk of arrhythmia, for example those on treatment for cardiovascular disease or who have thyroid disease
- dehydration
- severe acute inflammatory bowel disease
- pre-existing serum electrolyte disturbance

In debilitated fragile patients, patients with poor health, those with clinically significant renal impairment, arrhythmia and those at risk of electrolyte imbalance, the physician should consider performing a baseline and post-treatment electrolyte, renal function test, and ECG as appropriate.

There have been rare reports of serious arrhythmias including atrial fibrillation associated with the use of ionic osmotic laxatives for bowel preparations. These occur predominantly in patients with underlying cardiac risk factors and electrolyte disturbance.

Patients with insulin-dependent diabetes should consult their physician prior to use of MOVIPREP. Only liquids should be consumed during usage of MOVIPREP, therefore insulin dosing should be balanced accordingly.

The presence of dehydration should be corrected before the use of MOVIPREP.

Semi-conscious patients or patients prone to aspiration or regurgitation should be closely monitored during administration, especially if administered via nasogastric tube.

If patients develop any symptoms indicating arrhythmia or shifts of fluid/electrolytes (e.g. oedema, shortness of breath, increasing fatigue, or cardiac failure) plasma electrolytes should be measured, ECG monitored and any abnormality treated appropriately.

If a patient experiences severe bloating, abdominal distension, or abdominal pain, administration should be slowed or temporarily discontinued until the symptoms abate.

Ischaemic colitis

Post-marketing cases of ischaemic colitis, including serious cases, have been reported in patients treated with macrogol for bowel preparation. Macrogol should be used with caution in patients with known risk factors for ischaemic colitis or in case of concomitant use of stimulant laxatives (such as bisacodyl or sodium picosulfate). Patients presenting with sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis should be evaluated promptly.

This medicine contains 363.2 mmol (8.4 g) sodium per course of treatment. This should be taken into consideration by patients on a sodium controlled diet (see section 2, Qualitative and Qualitative Composition). Only a proportion of sodium is absorbed, (see section 5.2 Pharmacokinetic properties).

This medicine contains 28.4 mmol (1.1 g) potassium per course of treatment. This should be taken into consideration by patients with reduced kidney function or patients on a controlled potassium diet (see section 2, Qualitative and Qualitative Composition).

Contraceptive cover from the oral contraceptive pill is likely to be incomplete if it is taken at any time during the process of bowel cleansing with MOVIPREP (an hour before the first dose of MOVIPREP until after the investigation). Therefore an alternative method of contraception should be used for the length of the cycle when MOVIPREP is taken.

Use in the elderly

Use with caution in elderly or debilitated patients.

Paediatric Use

The safety and efficacy of MOVIPREP has not been studied in the paediatric population therefore it is not recommended for use in children below 18 years.

Effects on laboratory tests
No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS
Oral medication should not be taken within one hour of administration of MOVIPREP (i.e. includes one hour before administration, as well as during administration and one hour after administration), as it may be flushed from the gastrointestinal tract and not absorbed. Specific consideration should be given to sustained release formulations and products with a narrow therapeutic window. Please refer to Section 4.4 Special Warnings and Precautions for Use for advice on oral contraceptives.

MOVIPREP may have a potential interactive effect when 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
Effects on fertility
No data available.

Use in pregnancy
Pregnancy Category B1: Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have not shown evidence of an increased occurrence of fetal damage.

There is no experience of the use of MOVIPREP during pregnancy. MOVIPREP should only be used if considered essential by the physician.

Use in lactation
There is no experience of the use of MOVIPREP during lactation. MOVIPREP should only be used if considered essential by the physician.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)
Diarrhoea is an expected outcome of bowel preparation.

Due to the nature of the intervention, undesirable effects occur in the majority of patients during the process of bowel preparation. Whilst these vary between preparations, nausea, vomiting, bloating, abdominal pain, anal irritation and sleep disturbance commonly occur in patients undergoing bowel preparation. Dehydration may occur as a result of diarrhoea and/or vomiting.

As with other bowel cleansing products containing macrogol, allergic reactions including rash, urticaria, pruritus, dyspnoea, angioedema and anaphylaxis have been reported.

Data from clinical studies are available in a population of 825 patients treated with MOVIPREP in which undesirable effect data were actively elicited. Additionally, adverse events reported in post-marketing are included.

The frequency of adverse reactions to MOVIPREP is defined using the following convention:

Very common	≥ 1/10 (≥ 10%)
Common	≥ 1/100, < 1/10 (≥ 1%, < 10%)
Uncommon	≥ 1/1,000, < 1/100 (≥ 0.1%, < 1%)
Rare	≥ 1/10,000, < 1/1,000 (≥ 0.01%, < 0.1%)
Very rare	< 1/10,000 (< 0.01%)
Not known (cannot be estimated from the available data)	

Body System	**Frequency**	**Adverse Drug Reaction**
Immune system disorders	Not known	Allergic reaction including anaphylactic reaction, dyspnoea and skin reactions (see below)"
Metabolism and Nutrition Disorders	Not known	Electrolyte disturbances including blood bicarbonate decreased, hyper and hypo calcaemia, hypophosphataemia, hypokalaemia and hyponatraemia, and changes in the blood chloride level. Dehydration
Psychiatric disorders	Common	Sleep disorder.
Nervous system disorders	Common	Dizziness, headache.
	Not known	Convulsions associated with severe hyponatraemia.
Cardiac disorders	Not known	Transient increase in blood pressure. Arrhythmia, palpitations
Gastrointestinal disorders	Very common	Abdominal pain, nausea, abdominal distension, anal discomfort.
	Common	Vomiting, dyspepsia.
	Uncommon	Dysphagia.
	Not known	Flatulence, retching.
Hepatobiliary disorders	Uncommon	Abnormal liver function tests.
Skin and subcutaneous tissue disorders	Not known	Allergic skin reactions including angioedema, urticaria, pruritis, rash, erythema
General disorders and administration site conditions	Very common	Malaise, pyrexia
	Common	Rigors, thirst, hunger.

	Uncommon	Discomfort.

Reporting suspected adverse effects
Reporting suspected adverse reactions after registration of the medicine is important. It allows continued monitoring of the benefit-risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE
In case of gross accidental overdosage, where diarrhoea is severe, conservative measures are usually sufficient, generous amounts of fluid should be given. Further information on the latest overdosage treatment can be obtained by contacting the following Poisons Information Centres: 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES
Mechanism of action

Macrogol 3350, sodium sulfate and high doses of ascorbic acid exert an 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 a propulsive colonic transportation of the softened stools. The electrolytes present in the formulation and the supplementary clear liquid intake are included to prevent clinically significant variations in sodium, potassium or water, and therefore reduce dehydration risk.

Clinical Trials
No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption
Macrogol 3350 is unchanged along the gut. It is virtually unabsorbed from the gastrointestinal tract.

Ascorbic acid is absorbed mainly at the small intestine level by a mechanism of active transport, which is sodium dependent and saturable. There is an inverse relationship between the ingested dose and the percentage of the dose absorbed. For oral doses between 30 and 180 mg an amount of 70-85% of the dose is absorbed. Following oral intake of up to 12 g ascorbic acid, it is known that only 2 g is absorbed.

Excretion
Any macrogol 3350 that is absorbed is excreted via the urine.

After high oral doses of ascorbic acid and when plasma concentrations exceed about 15 mg/L, the absorbed ascorbic acid is mainly eliminated unchanged in the urine.

The pharmacokinetics of MOVIPREP have not been studied in patients with renal or hepatic insufficiency.

Osmotically-acting bowel preparations lead to a copious diarrhoea, resulting in extensive elimination of most of the product via the faeces. They can also lead to changes in electrolyte balance in the body, often with depletion of sodium and potassium, the additional sodium and potassium included in the MOVIPREP formulation help to balance the electrolytes. While some absorption of sodium takes place, the bulk of sodium is expected to be excreted in the faeces as the sodium salts of sulfate and ascorbate, the osmotic active ingredients included in the MOVIPREP composition.

5.3 PRECLINICAL SAFETY DATA

Preclinical studies show that macrogol 3350, ascorbic acid, and sodium sulfate have no significant systemic toxicity potential.
Both sodium chloride and potassium chloride are present at a similar level to normal daily intake from the diet.

Genotoxicity

No studies have been carried out on the genotoxicity of the product.
However, available data on macrogols of relevant size did not identify any potential genotoxicity or reproductive toxicity.

Sodium sulfate showed negative results in genotoxicity and reproductive toxicity studies.

Ascorbic acid showed negative results in assessments of genotoxicity and reproductive toxicity.

Carcinogenicity

No studies have been carried out on the carcinogenicity of the product.
However, available data on macrogols of relevant size did not identify any potential carcinogenicity toxicity.

Ascorbic acid showed negative results in assessments of carcinogenicity.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Aspartame, acesulfame potassium, and lemon flavour (contains maltodextrin, citral, lemon oil, lime oil, xanthan gum, vitamin E).

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

Sachets: Shelf life 3 years
Reconstituted solution: 24 hours.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Sachets : Store below 25°C.

Reconstituted solution: Store below 25°C, or store in refrigerator. Keep solution covered.

6.5 NATURE AND CONTENTS OF CONTAINER

One pack of MOVIPREP contains a single treatment of two bags. Each bag contains one Sachet A containing 112 g of powder, and one Sachet B containing 11 g of powder.

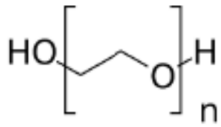
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical Structure

Macrogol 3350



Ascorbic acid	$C_6H_8O_6$
Sodium chloride	NaCl
Sodium sulfate	Na_2SO_4
Potassium chloride	KCl
Sodium ascorbate	$NaC_6H_7O_6$

CAS Number

Ascorbic acid	50-81-7
Macrogol 3350	25322-68-3
Sodium chloride	7647-14-5
Sodium sulfate	7757-82-6
Potassium chloride	7447-40-7
Sodium ascorbate	134-03-2

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 3 - Pharmacist Only Medicine

8 SPONSOR

Norgine Pty Limited
Suite 3.01 Building A
20 Rodborough Road
Frenchs Forest NSW 2086

9 DATE OF FIRST APPROVAL

25 September 2008

10 DATE OF REVISION

03 May 2023

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
2	Changed ascorbate electrolyte ion concentration.
4.5	Statement added to clarify the meaning of “within one hour”.