New Zealand Datasheet

1 PRODUCT NAME
PLENVU

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
PLENVU is a powder for oral solution contained in three separate sachets. The first dose is supplied in one sachet and the second dose is supplied in two sachets, A and B.

Dose 1 sachet contains the following active substances:

Macrogol 3350	100.0 g
Sodium sulfate	9.0 g
Sodium chloride	2.0 g
Potassium chloride	1.0 g

The concentration of electrolyte ions when the first dose is made up to 500 mL of solution is as follows:

Sodium	160.9 mmol/500 mL
Sulfate	63.4 mmol/500 mL
Chloride	47.6 mmol/500 mL
Potassium	13.3 mmol/500 mL

Dose 1 also contains 0.79 g of sucralose (E955).

Dose 2 (Sachets A and B) contains the following active substances:

Sachet A:

Macrogol 3350	40.0 g
Sodium chloride	3.2 g
Potassium chloride	1.2 g

Sachet B:

Sodium ascorbate	48.1 g
Ascorbic acid	7.5 g

The concentration of electrolyte ions when the second dose (Sachets A and B) is made up to 500 mL of solution is as follows:

Sodium	297.6 mmol/500 mL
Ascorbate	285.7 mmol/500 mL
Chloride	70.9 mmol/500 mL
Potassium	16.1 mmol/500 mL

Dose 2 (Sachet A) also contains 0.88 g of aspartame (E951).

3 PHARMACEUTICAL FORM
Powder for oral solution.
White to yellow powders.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

PLENVU is indicated for bowel cleansing prior to any procedure requiring a clean bowel.

4.2 Dose and method of administration

Adults (18 years of age and over) and elderly

A course of treatment consists of two separate non-identical 500 mL doses of PLENVU. At least 500 mL of additional clear fluid, which may include water, clear soup, fruit juice without pulp, soft drinks, tea and/or coffee without milk, must be taken with each dose.

This course of treatment can be taken according to one of the three schedules specified below:

- Two-day split dosing schedule with the first 500 mL dose of PLENVU (including additional 500 mL of clear fluid) taken in the evening before the clinical procedure and the second 500 mL dose (including an additional 500 mL of clear fluid) in the morning of the day of the clinical procedure (approximately 12 hours after the start of the first dose), or
- Morning only dosing schedule with both doses taken in the morning of the day of the clinical procedure (including an additional 500 mL of clear fluid); the second dose should be taken a minimum of 2 hours after the start of the first dose, or
- Day before dosing schedule with both doses taken in the evening before the clinical procedure (including an additional 500 mL of clear fluid); the second dose should be taken a minimum of 2 hours after the start of the first dose.

A time interval of more than 12 hours between preparation administration and colonoscopy may reduce the bowel cleansing efficacy.

The appropriate dosing schedule should be selected according to the timing of the clinical procedure.

Patient should be warned to expect frequent, loose bowel movements.

Patients should be reminded of the importance of hydration while taking these products and to seek medical attention if they experience any signs of severe dehydration, such as excessive thirst, dizziness, confusion and decreased urine output or dark coloured urine.

Paediatric population

The safety and efficacy of PLENVU in children below 18 years of age has not yet been established. PLENVU is therefore not recommended for use in this population.

Patients with renal impairment

No special dosage adjustment of PLENVU is deemed necessary in patients with mild to moderate renal impairment. Patients with mild to moderate renal impairment were included in clinical studies.

Patients with hepatic impairment

No special dosage adjustment of PLENVU is deemed necessary in patients with mild to moderate hepatic impairment. Patients with elevated liver function tests were included in clinical studies.

Preparation Instructions

Dose 1: The contents of the single sachet for Dose 1 should be made up to 500 mL with water (not chilled). The reconstituted solution, plus an additional 500 mL of clear fluid, should be

taken over a period of 60 minutes. Alternating between the reconstituted solution and the clear fluid is acceptable.

Dose 2: The contents of the two sachets (sachets A and B together) for Dose 2 should be made up to 500 mL with water (not chilled). The reconstituted solution, plus an additional 500 mL of clear fluid, should be taken over a period of 60 minutes. Alternating between the reconstituted solution and the clear fluid is acceptable.

In some instances, the intake of the reconstituted solution may be slowed or temporarily discontinued (see section 4.4).

Reconstitution of PLENVU in water (not chilled) may take up to approximately 8 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 in water PLENVU consumption may begin immediately or if preferred, it may be refrigerated before use.

In addition to the fluids taken as part of the course of treatment, any amount of supplementary clear fluid (e.g. water, clear soup, fruit juice without pulp, soft drinks, tea and/or coffee without milk) may be taken throughout the bowel preparation process. Note: Patients should avoid any fluid coloured red or purple (e.g. blackcurrant juice) as this can stain the bowel.

Consumption of all fluids should be stopped at least:

- two hours before the start of the clinical procedure when under general anaesthesia, or
- one hour before the clinical procedure without general anaesthesia.

Information regarding meals

Two-day split dosing schedule and day before dosing schedule:

The day before the clinical procedure, patients can have a light breakfast followed by a light lunch which must be completed at least 3 hours prior to the start of the first dose. No solid food should be taken from the start of the course of treatment until after the clinical procedure.

Morning only dosing schedule:

The day before the clinical procedure, patients can have a light breakfast followed by a light lunch, and clear soup and/or plain yogurt for dinner, which should be completed by approximately 8pm. No solid food should be taken from the start of the course of treatment until after the clinical procedure.

Patients should be advised to allow adequate time after bowel movements have subsided to travel to the clinical unit.

4.3 Contraindications

Do not use in patients with known or suspected:

- hypersensitivity to the active or inactive ingredients
- gastrointestinal obstruction or perforation
- ileus
- disorders of gastric emptying (e.g. gastroparesis, gastric retention, etc.)
- phenylketonuria (due to the presence of aspartame)
- glucose-6-phosphate dehydrogenase deficiency (patients may be at risk of acute haemolysis due to the presence of ascorbate)
- unconsciousness
- severe dehydration

- severe inflammatory conditions of the intestinal tract, such as Crohn's disease, ulcerative colitis and toxic megacolon

4.4 Special warnings and precautions for use

The fluid content of PLENVU when reconstituted with water does not replace regular fluid intake and adequate fluid intake must be maintained.

As with other macrogol containing products, allergic reactions including rash, urticaria, pruritus, angioedema and anaphylaxis are a possibility.

Caution should be used with the administration of PLENVU to frail or debilitated patients.

PLENVU should also be used with caution in patients with:

- impaired gag reflex, with the possibility of regurgitation or aspiration, or with diminished levels of consciousness. Such patients should be closely observed during administration especially if given via a nasogastric route
- renal impairment whose creatinine clearance is less than 30 mL/minute/1.73 m^2
- grade III or IV cardiac failure
- those at risk of arrhythmia, for example those on treatment for cardiovascular disease or who have thyroid disease

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. Any suspected dehydration should be corrected for before use of PLENVU.

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

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

If patients experience severe bloating, abdominal distension, or abdominal pain, administration should be slowed or temporarily discontinued until the symptoms subside.

<u>Ischaemic colitis</u>

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.

In patients with mild to moderate hepatic impairment no special dosage adjustment of PLENVU is deemed necessary. Patients with elevated liver function tests were included in clinical studies.

PLENVU contains 458.5 mmol (10.5 g) sodium per course of treatment. This should be taken into consideration for patients on a controlled sodium diet. Only a proportion of the sodium is absorbed.

PLENVU contains 29.4 mmol (1.15 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.

Paediatric Use
The safety and efficacy of PLENVU in children below 18 years of age has not yet been established. PLENVU is therefore not recommended for use in this population.

4.5 Interaction with other medicines and other forms of interaction
The interaction of PLENVU with other medicinal products has not been studied. Theoretically, medicinal products taken orally (e.g. oral contraceptive pill) one hour before, during and one hour after PLENVU administration may be flushed from the gastrointestinal tract unabsorbed.

Medications such as diuretics, calcium channel blockers or corticosteroids, may affect electrolyte levels or may exacerbate hypokalaemia.

Medications such as diuretics may exacerbate volume depletion associated with bowel cleansing.

PLENVU 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.

For more information, refer to section 4.4.

4.6 Fertility, pregnancy and lactation
There are no data on the effects of PLENVU on fertility.

Use in Pregnancy
There are no data on the use of PLENVU during pregnancy. The preparation should only be used during pregnancy or lactation if considered essential by the physician.

Use in Lactation
There are no data on the use of PLENVU during lactation. The preparation should only be used during pregnancy or lactation if considered essential by the physician.

4.7 Effects on ability to drive and use machines
PLENVU has no influence on the ability to drive and use machines.

4.8 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.

Data from clinical studies are available in a population of over a thousand subjects treated with PLENVU in which undesirable effect data were actively elicited.

The table below is a list of treatment emergent adverse events reported in the clinical studies of PLENVU.

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

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

	Very common (≥ 1/10) #	Common (≥ 1/100 to <1/10)	Uncommon (≥ 1/1,000 to <1/100)
Gastrointestinal disorders		Vomiting, Nausea	Abdominal distension, Anorectal discomfort, Abdominal pain, Abdominal pain upper, Abdominal pain lower
Immune system disorders			Drug hypersensitivity
Metabolism and nutrition disorders		Dehydration	
Nervous system disorders			Headache, Migraine, Somnolence
General disorders and administration site conditions			Thirst*, Fatigue, Asthenia, Chills**, Pains, Aches
Cardiac disorders			Palpitation, Sinus tachycardia
Vascular disorders			Transient increase in blood pressure, Hot flush
Investigations			Transient increase in liver enzymes*** Hypernatraemia, Hypercalcaemia, Hypophosphataemia, Hypokalaemia, Decreased bicarbonate, Anion gap increased/ decreased, Hyperosmolar state

*Thirst includes the Preferred Terms; Thirst, Dry mouth and Dry throat
**Chills includes the Preferred Terms; Chills, Feeling hot and Feeling cold
***Transient increase in liver enzymes includes the Preferred Terms; ALT increased, AST increased, GGT increased, Hepatic enzymes increased, Transaminases increased
No adverse events with a frequency of "very common" were reported during the clinical trials.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose

Overdosage may cause severe diarrhoea. In case of overdose, fluid replacement and electrolyte correction may be necessary. For information on the management of overdose, contact the Poisons Information Centre on 0800 764 766.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Osmotically acting laxative. ATC code: A06A D65.

The pharmacodynamic properties of this osmotically-acting bowel preparation are a combination of the direct synergistic osmotic action of the components of PLENVU (macrogol 3350 plus sodium sulfate components in Dose 1 and ascorbate plus macrogol 3350 components in Dose 2) and the induction of propulsive contractions of the smooth muscle of the bowel, which induce the laxative effect. The physiological consequence is a propulsive colonic transportation of the softened stools.

The electrolytes present in the formulation and the supplementary clear fluid intake are included to prevent clinically significant variations of sodium, potassium or water, and thus reduce dehydration risk.

Macrogol 3350 is chemically inert and highly soluble in water. The principal action of macrogol 3350 is to increase the water content of the bowel by exerting an osmotic action. Macrogol 3350 is able to hold water in the ratio of 100 molecules of water to every one molecule of macrogol 3350 and it has been shown that increasing osmotic loads of macrogol 3350 results in a near linear increase in stool weight and stool water output.

The osmotic effect of ascorbate is based on the fraction that is not absorbed; the inclusion of ascorbic acid and sodium ascorbate into a single dose is intended to limit absorption and maximise this osmotic effect. Oral ascorbate doses above 2 g undergo very little systemic absorption, and the bulk administered is present in the colon.

The bulk of sulfate is not absorbed and remains in the intestine adding to the synergistic osmotic action in Dose 1. The osmotic action of sodium sulfate is brought about by irritation of the intestinal mucosa by high intraluminal concentrations of sulfate ions.

Clinical Trials
The colon cleansing efficacy, safety and tolerability of PLENVU was evaluated in three randomized, parallel group, multi-centre, investigator-blinded, Phase III studies in patients undergoing colonoscopy.

The three studies, NER1006-01/2014 (NOCT), NER1006-02/2014 (MORA) and NER1006-03/2014 (DAYB) were designed with many similarities to allow for optimum comparability of data. The primary focus of the Phase III clinical program was to compare the bowel cleansing ability of PLENVU against a different comparator using different dosing regimen(s):

- Two-Day split-dosing allowing for an overnight gap between doses,
- One-Day Morning dosing giving both doses the morning of the day of colonoscopy and
- One-Day Day Before dosing giving both doses the day before colonoscopy.

Details of which regimen was used in each study for PLENVU and each of the comparators are provided in Table 1.

Table 1: PLENVU and comparator dosing regimens in NOCT, MORA and DAYB studies

	Phase III Study		
Treatment	**NOCT**	**MORA**	**DAYB**
PLENVU			
Two-Day split-dosing	x	x	
One-Day Morning dosing (day of colonoscopy)		x	
One-Day Day Before dosing (day before colonoscopy)			x
Comparator:			
Two-Day split-dosing	x (Trisulfate)	x (2L PEG+E) MOVIPREP	
One-Day Day Before split-dosing (day before colonoscopy)			x (SP+MS)

(SP+MS) = Sodium Picosulfate and Magnesium Salt solution; (PEG+E) = PEG and Electrolytes

Design of Studies
The alternative primary endpoints were the same across all three studies and were as follows:

- The overall bowel cleansing success rate of PLENVU is non-inferior to that of the comparator using the Harefield Cleansing Scale (HCS), wherein success corresponds to Grades A and B, and failure corresponds to Grades C and D.

- The 'Excellent plus Good' cleansing rate in the ascending colon of PLENVU is non-inferior to that of the comparator using the segmental cleansing scoring system of the HCS, wherein the ordinal score of 4 corresponds to Excellent cleansing and score of 3 corresponds to Good cleansing.

The alternative primary efficacy endpoint was judged by blinded central readers (gastroenterologists) on the basis of video recordings of the colonoscopy.
The patient population consisted of male and female patients aged 18 to 85 years inclusive, who were scheduled to undergo a screening, surveillance or diagnostic colonoscopy.

NOCT Study
The NOCT study was a multicentre, randomized, parallel group Phase III study comparing the bowel cleansing efficacy, safety and tolerability of PLENVU versus a trisulfate bowel cleansing solution containing sodium sulfate, potassium sulfate, and magnesium sulfate using an overnight Two-Day split-dosing regimen in adults.

A total of 516 patients [255 patients in the PLENVU treatment group and 261 patients in the trisulfate solution treatment group] completed the study. Overall, the demographic characteristics were well balanced between the two treatment groups.

A similar percentage of patients achieved successful bowel cleansing in the overall colon in both treatment groups (85.1% in the PLENVU treatment group versus 85.0% in the trisulfate solution treatment group). With regard to the cleansing rate in the ascending colon, a greater percentage of patients achieved an "Excellent plus Good" cleansing rate in the PLENVU treatment group (35.9% in the PLENVU treatment group versus 29.3% in the trisulfate solution treatment group). PLENVU was shown to be non-inferior to the trisulfate solution with regard to both alternative primary endpoints of HCS results in the overall colon and the ascending colon.

MORA Study
The MORA study was a multicentre**,** randomised, parallel group Phase III study in adults comparing the bowel cleansing efficacy, safety and tolerability of PLENVU **(**Two-Day split-dosing and One-Day Morning dosing regimens**)** versus a 2 litre PEG + electrolytes (MOVIPREP) Two-Day split-dosing regimen**.**

A total of 781 patients [260 patients in the Two-Day PLENVU split-dosing group, 262 in the One-Day PLENVU morning dosing group and 259 patients in the 2L PEG+E treatment group] completed the study. Overall, the demographic characteristics were well balanced between the three treatment groups.

Similar percentages of patients achieved a successful bowel cleansing in the overall colon in the three treatment groups (92.0% in the PLENVU 2-day split-dosing group, 89.1% in the PLENVU 1-day split-dosing group and 87.5% in the 2L PEG+E treatment group), confirming non-inferiority for the PLENVU Two-Day split-dosing and PLENVU One-Day split-dosing groups versus the 2L PEG+E group. With regard to the cleansing rate in the ascending colon, both PLENVU groups met the criteria for superiority versus the 2L PEG+E group. The PLENVU Two-Day and One-Day dosing groups achieved "Excellent plus Good" cleansing rates of 31.6% and 33.8% respectively, whilst the 2L PEG+E group achieved a rate of 15.1%.

DAYB Study

The DAYB study was a multicentre, randomized, parallel group Phase III study comparing the bowel cleansing efficacy, safety and tolerability of PLENVU versus a Sodium Picosulfate and Magnesium Salt (SP+MS) solution, using a One-Day Day Before dosing regimen in adults.

A total of 473 patients [233 patients in the PLENVU treatment group, and 240 patients in the SP+MS treatment group] completed the study. Overall, the demographic characteristics were well balanced between the two treatment groups.

A higher percentage of patients achieved successful bowel cleansing in the overall colon in the PLENVU group compared to the SP+MS group (62.0% versus 53.8% respectively), however this did not reach statistical significance. Regarding the cleansing rate in the ascending colon, a similar percentage of patients achieved an "Excellent plus Good" cleansing rate (4.4% in the PLENVU treatment group versus 1.2% in the SP+MS treatment group). PLENVU was shown to be non-inferior to SP+MS with regard to both alternative primary endpoints in the overall colon and the ascending colon.

Demographics and Results

In general, the demographic characteristics were well balanced across the PLENVU patients in all three studies. However, there were two notable differences in 1) patients aged over 65: MORA (26% Two-Day and 22% One-Day), NOCT (18%) and DAYB (17%) and 2) the ratio of female and male patients: MORA (males 42% Two-Day and 46% One-Day), NOCT (males 51%) and DAYB (males 35%).

The alternative primary endpoint results are provided in Table 2.

Table 2: Overall and Ascending Colon Cleansing rates of PLENVU versus Comparator

Studies		**NOCT**		**MORA**			**DAYB**	
Comparators		**PLENVU**	**Trisulfate**	**PLENVU 2-Day**	**PLENVU 1-Day**	**2L PEG+E**	**PLENVU**	**SP+MS**
Regimen		Two-Day Split-Dosing	Two-Day Split-Dosing	Two-Day Split-Dosing	One-Day Morning of Colonoscopy Dosing	Two-Day Split-Dosing	One-Day Day Before Colonoscopy Dosing	One-Day Day Before Colonoscopy Dosing
Alternative Primary Endpoints using HCS	Overall Colon Cleansing Rate	85.1 %	85.0%	92.0%	89.1%	87.5%	62.0%	53.8%
		(LCL= -8.15, p=0.528)		(LCL=-4.00, p=0.055)	(LCL=-6.91, p=0.328)		(LCL=-0.50, p=0.038)	
	Ascending Colon Cleansing Rate (Excellent plus Good)	35.9%	29.3%	31.6%	33.8%	15.1%	4.4%	1.2%
		(LCL=-1.69, p=0.059)		(LCL=8.11, p<0.001)	(LCL=10.32, p<0.001)		(LCL=-5.56, p=0.027)	
Summary of Primary Endpoints		Non-inferiority demonstrated - Primary endpoints met		Non-inferiority demonstrated - Primary endpoints met. Superiority for Excellent + Good ascending colon cleansing demonstrated			Non-inferiority demonstrated - Primary endpoints met	

LCL= 97.5% Lower Confidence Limit
10% NI margin; threshold for statistical significance: p<0.025

5.2 Pharmacokinetic properties

The vast majority (>99.7%) of macrogol 3350 is not absorbed by the gastro-intestinal tract and is excreted in faeces. Literature reports that any macrogol 3350 that is absorbed is excreted via the urine.

Absorption of ascorbate occurs by a sodium-dependent active transport process of limited

capacity; a single oral dose above 2 g is reported to saturate jejunal absorption. The unabsorbed ascorbate remains in the gut lumen, it is estimated approximately 96% (48 g) of the ascorbate component is excreted in faeces. Ascorbate is a normal constituent of the blood, however when plasma concentrations exceed approximately 15 µg/mL, excess ascorbic acid is eliminated, mainly unchanged, in the urine.

The bulk of oral sulfate is not absorbed, and by establishing an electrochemical gradient, prevents the absorption of accompanying sodium ions. Small amounts of sulfate ions are absorbed throughout the gastrointestinal tract, which adds to the pool of essential inorganic sulfate formed from the breakdown of sulfur containing amino acids. The bulk of absorbed inorganic sulfate is eliminated unchanged by glomerular filtration and is subject to saturable tubular reabsorption.

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 PLENVU 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 PLENVU composition.

No pharmacokinetic studies were performed in patients with renal or hepatic insufficiency.

5.3 Preclinical safety data

Preclinical studies provide evidence that macrogol 3350, ascorbic acid and sodium sulfate have no significant systemic toxicity potential.

No studies have been carried out on the genotoxicity, carcinogenicity, or toxic effect on reproduction with this product.

However, available data on macrogols of relevant size, sodium sulfate and ascorbic acid did not reveal any special hazard for humans based on studies of genotoxicity, carcinogenicity and reproductive toxicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

PLENVU contains the following inactive ingredients: sucralose (E955), aspartame (E951) encapsulated citric acid (contains citric acid and maltodextrin), mango flavour and fruit punch flavour.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Sachets: 24 months (2 years) from manufacture.
Reconstituted solutions: 24 hours

6.4 Special precautions for storage

Sachets: Store below 25°C.

Reconstituted solutions: Store below 25°C, or store in refrigerator. Keep solutions covered. Shelf life of solutions is 24 hours.

6.5 Nature and contents of container

One pack of PLENVU contains a single treatment of three sachets.
Dose 1 (mango flavour) contains 115.96 g of powder.
Dose 2 (fruit punch flavour) Sachet A contains 46.26 g of powder and Dose 2 Sachet B contains 55.65 g of powder.

The three sachets are contained in a clear secondary overwrap within a cardboard carton. The cardboard carton also contains the patient information leaflet.

6.6 Special precautions for disposal
No special precautions required.

7 MEDICINE SCHEDULE
Pharmacist-Only Medicine.

8 SPONSOR
Sponsor:
CARSL Consulting
PO Box 766
Hastings
Ph (06) 875 0979
for Norgine Pty Limited
0800 404178

Distributor:
Pharmacy Retailing (NZ) Ltd
Trading as Healthcare Logistics
58 Richard Pearse Drive
Airport Oaks
PO Box 62-027
Mt Wellington
Auckland
Telephone: (09) 918 5100
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9 DATE OF FIRST APPROVAL
16 May 2019

10 DATE OF REVISION OF THE TEXT
1 May 2024

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
4.5	Section 4.5 was updated to clarify the theoretical nature of the one-hour time interval between taking macrogol-containing products and taking other oral medicinal products.