1 OSMITROL (solution for infusion)

Osmitrol 10%
Osmitrol 20%

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient
Mannitol.

Osmitrol infusion solution (mannitol intravenous infusion, BP) contains mannitol. It contains no antimicrobial agents.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion.

Osmitrol is a clear, colourless solution free from visible particles.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Osmitrol infusion solution (mannitol intravenous infusion, BP) can be used in:

- The promotion of diuresis, in the prevention and/or treatment of the oliguric phase of acute renal failure before irreversible renal failure becomes established;
- The reduction of elevated intraocular pressure when the pressure cannot be lowered by other means;
- The reduction of intracranial pressure and treatment of cerebral oedema by reducing brain mass and;
- Promoting the urinary excretion of toxic substances.

4.2 Dose and method of administration

Dosage
Osmitrol infusion solution (mannitol intravenous infusion, BP) should be administered only by intravenous infusion. The total dosage, concentration, and rate of administration should be governed by the nature and severity of the condition being treated, fluid requirement, and urinary output. There should be a dosage limit of 50g of Osmitrol on any one occasion. The usual adult dosage ranges from 20 to 100g in a 24 hour period, but in most instances an adequate response will be achieved at a dosage of approximately 50 to 100g in a 24 hour period. The rate of administration is usually adjusted to maintain a urine flow of at least 30 to 50mL/hour. This outline of administration and dosage is only a general guide to therapy.

Parenteral medicine products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit. Use of a final filter is recommended during administration of all parenteral solutions, where possible.

Test dose: A test dose of mannitol should be given prior to instituting Osmitrol intravenous infusion (mannitol intravenous infusion, BP) therapy for patients with marked oliguria, or those believed to have inadequate renal function. Such a test dose may be approximately 0.2g/kg body weight (about 75mL of a 20% solution) infused in a period of three to five minutes to produce a urine flow of at least 30 to 50mL/hour. If urine flow does not increase, a second test dose may be given; if there is an inadequate response, the patient should be re-evaluated.

Prevention of acute renal failure (oliguria): When used during cardiovascular and other types of surgery, 50 to 100g of mannitol as a 10% or 20% solution may be given. The concentration will depend upon the fluid requirements of the patient.

Treatment of oliguria: The usual dose for treatment of oliguria is 100g administered as a 20% solution.

Reduction of intraocular pressure: A dose of 1.5 to 2.0g/kg as a 20% solution (7.5 to 10mL/kg) may be given over a period as short as 30 minutes in order to obtain a prompt and maximum effect. When used pre-operatively the dose should be given one to one and a half hours before surgery to achieve maximum reduction of intraocular pressure before operation.

Reduction of intracranial pressure: Usually a maximum reduction in intracranial pressure in adults can be achieved with a dose of 0.25g per kg given not more frequently than every six to eight hours. An osmotic gradient between the blood and cerebrospinal fluid of approximately 10mOsml per litre will yield a satisfactory reduction in intracranial pressure.

Adjunctive therapy for intoxication: As an agent to promote diuresis in intoxications, 10% or 20% mannitol is indicated. The concentration will depend upon the fluid requirement and urinary output of the patient. Measurement of glomerular filtration rate by creatinine clearance may be useful for determination of dosage.

All IV Infusions in Viaflex containers are intended for intravenous administration using sterile equipment.

Directions for use
Warning: Mannitol solutions may crystallize when exposed to low temperature. At higher concentrations, the solutions have a greater tendency to crystallize. Inspect for crystals prior to administration. If crystals are visible, re-dissolve by warming the solution up to 70°C, with agitation. The recommended method is to use dry heat e.g. warming pad. Solutions should not be heated in water or in a microwave oven due to the potential for product contamination or damage. Allow the solution to cool to room or body temperature before re-inspection for crystals and use.

Do not use plastic container in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is completed.

Pressurising intravenous solutions contained in flexible plastic containers to increase flow rate can result in air embolism if the residual air in the container is not fully evacuated prior to administration.

Use of a vented intravenous administration set with the vent in the open position could results in air embolism. Vented intravenous administration sets with the vent in the open position should not be used in flexible plastic container.

To open: Tear overwrap down side at slit and remove solution container. Some opacity of the plastic due to moisture absorption during the sterilisation process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually. Check for minute leaks by squeezing the inner bag firmly. If leaks are found, discard solution as sterility may be impaired.

Preparation for Administration

- Suspend container from eyelet support, at bottom of container.
- Remove plastic protector from outlet port at bottom of container.
- Attach administration set. Refer to complete directions accompanying set.

4.3 Contraindications

Osmitrol infusion solution (mannitol intravenous infusion, BP) is contraindicated in patients with:

- Hypersensitivity to mannitol
- Pre-existing plasma hyperosmolarity
- Severe heart failure
- Disturbance of the blood-brain barrier
- Well established anuria due to severe renal disease
- No response to test dose
- Severe pulmonary congestion or frank pulmonary oedema
- Active intracranial bleeding except during craniotomy
- Severe dehydration
- Progressive renal damage or dysfunction after institution of mannitol therapy, including increasing oliguria and azotemia, and
- Progressive heart failure or pulmonary congestion after institution of mannitol therapy.

4.4 Special warnings and precautions for use

General

Osmitrol is hypertonic. Hypertonic solutions should be administered via a large peripheral and preferably central vein. Rapid infusion in peripheral veins may be harmful.

Hypersensitivity

Anaphylactic/anaphylactoid reactions, including anaphylaxis, as well as other hypersensitivity/ infusion reactions have been reported with mannitol. Fatal outcome has been reported (see section 4.8).

The infusion must be stopped immediately if any signs or symptoms of a suspected hypersensitivity reaction develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Risk of renal complications

Reversible, acute oligoanuric renal failure has occurred in patients with normal pre-treatment renal function who received large intravenous doses of mannitol.

In patients with severe impairment of renal function, a test dose should be utilised (see section 4.2). A second test dose may be tried if there is inadequate response, but no more than two test doses should be attempted.

Patients with pre-existing renal disease, or those receiving potentially nephrotoxic drugs, are at increased risk of renal failure following administration of Osmitrol. Serum osmolarity, urine flow and renal function should be monitored particularly closely.

The acid base, renal function and serum osmolarity must be monitored carefully when Osmitrol is used. Should patient serum osmolarity increase during treatment, the effects of Osmitrol on diuresis and reduction of intracranial and intraocular pressures may be impaired.

Osmotic nephrosis, a reversible vacuolisation of the tubules of unknown clinical significance, may proceed to severe irreversible nephrosis, so that the renal function must be closely monitored during mannitol infusion.

If urine output continues to decline during mannitol infusion, the patient's clinical status should be closely reviewed and mannitol infusion suspended if necessary. Accumulation of mannitol may result in overexpansion of the extracellular fluid, which may intensify existing or latent congestive heart failure.

CNS toxicity
CNS toxicity manifested by, e.g. confusion, lethargy and coma has been reported in patients treated with mannitol, in particular in the presence of impaired renal function. Fatal outcomes have been reported.

CNS toxicity may result from:

- High serum mannitol concentrations
- Serum hyperosmolarity resulting in intracellular dehydration within the CNS
- Hyponatraemia or other disturbances of electrolyte and acid/base balance
- Secondary to mannitol administration.

At high concentrations, mannitol may cross the blood brain barrier and interfere with the ability of the brain to maintain the pH of the cerebrospinal fluid especially in the presence of acidosis.

A rebound increase in intracranial pressure may occur approximately 12 hours after the use of mannitol for the reduction of intracranial pressure.

The use of mannitol in acute traumatic brain injury and acute stroke is not recommended. This is based on 2 Systematic Reviews that indicate the potential for harm and lack of sufficient data for a definitive assessment of the risk or benefit for using mannitol in these two clinical conditions.

Risk of water and electrolyte imbalances, hyperosmolarity
The obligatory diuretic response following rapid infusion of a 20% mannitol intravenous infusion may further aggravate pre-existing haemoconcentration. Excessive loss of water and electrolytes, may lead to serious imbalances such as hypernatraemia. Electrolyte measurements, including serum sodium and potassium are of vital importance and should be carefully monitored during mannitol administration.

Mannitol-induced osmotic diuresis may cause or worsen dehydration/hypovolaemia and haemoconcentration.

Osmitrol should not be administered in patients with shock and renal dysfunction until volume (fluid; blood) and electrolytes have been replaced.

In addition, depending on dosage and duration of administration, electrolyte and acid/base imbalances may result from transcellular shifts of water and electrolytes, osmotic diuresis and/or other mechanisms. Such imbalances may be severe and potentially fatal.

Imbalances that may result from mannitol treatment include:

- Hypernatraemia, dehydration and haemoconcentration
- Hyponatraemia - can lead to headache, nausea, seizures, lethargy, coma, cerebral oedema, and death. Acute Symptomatic Hyponatraemic Encephalopathy is considered a medical emergency. The risk for developing hyponatraemia is increased, for example in children, elderly patients, women, postoperatively and in persons with psychogenic polydipsia. The risk for developing encephalopathy as a complication of hyponatraemia is increased, for example in paediatric patients (≤ 16 years of age), women (in particular, premenopausal women), patients with hypoxaemia and patients with underlying central nervous system disease.
- Hypokalaemia
- Hyperkalaemia
- Other electrolytes imbalances
- Metabolic acidosis
- Metabolic alkalosis

By sustaining diuresis, mannitol administration may obscure and intensify inadequate hydration or hypovolaemia.

The use of supplemental additive medication is not recommended.

Risk of hypervolaemia
The cardiovascular status of the patient should be carefully evaluated before rapidly administrating mannitol since sudden expansion of the extracellular fluid may lead to fulminating congestive heart failure.

Shift of sodium free intracellular fluid into the extracellular compartment following mannitol infusion may lower serum sodium concentration and aggravate pre-existing hyponatraemia.

Patients receiving Osmitrol should be monitored for any deterioration in renal, cardiac or pulmonary function and treatment discontinued in the case of adverse events.

Crystallisation
When exposed to low temperatures, solutions of mannitol may crystallise. Concentrations of 20% have a greater tendency to crystallisation. Inspect for crystals prior to administration. If crystals are visible, redissolve by warming the solution up to 70°C, with agitation. The recommended method is to use dry heat e.g. warming pad. Solutions should not be heated in water or in a microwave oven due to the potential for product contamination or damage. Allow the solution to cool to room temperature before reinspection for crystals. Administer intravenously using a sterile, filter-type set.

Infusion site reactions
Infusion site reactions have occurred with the use of mannitol including signs and symptoms of infusion site irritation and inflammation as well as severe reactions (compartment syndrome and bullous eruptions) when associated with extravasation.

Laboratory tests
Although blood levels of mannitol can be measured there is little if any clinical virtue in doing so. The appropriate monitoring of blood levels of sodium and potassium; degree of haemoconcentration and haemodilution, if any, indices of renal, cardiac and pulmonary function are paramount in avoiding excess fluid and electrolyte shifts. The routine features of physical examination and clinical chemistries suffice in achieving an adequate degree of appropriate patient monitoring.

Mannitol can cause false low results in some tests systems for inorganic phosphorus blood concentrations.

Mannitol produces false positive results in tests for blood ethylene glycol concentrations in which mannitol is initially oxidised to an aldehyde.

Usage in children
Dosage requirements for patients 12 years of age and under have not been established. Safety and effectiveness in this population have not been established.

Usage in geriatrics
As for adults, the dosage depends on the weight, clinical and biological condition of the patient and concomitant therapy. The general dose range is the same as for adults (50 to 200g in 24-hour period), with a dosage limit of 50g on any one occasion. Since incipient renal insufficiency may be present, caution should be used when reviewing patient's status prior to dose selection.

4.5 Interaction with other medicines and other forms of interaction

Potentiation effects	concurrent use of other diuretics may potentiate the effects of mannitol and dose adjustments may be required.
Inhibition effects	concomitant use of mannitol impairs the response to lithium and methotrexate due to the increases in urinary excretion.
Cumulative nephrotoxicity	patients receiving concomitant cyclosporin should be closely monitored for signs of nephrotoxicity.
Other potential interactions	caution regarding concomitant use with aminoglycosides (potentiation of ototoxic effects), depolarising neuromuscular blocking agents (enhancement of their effects), oral anti-coagulants (reduce their effects by increasing concentration of clothing factors secondary to dehydration), and digoxin (digoxin toxicity if hypokalaemia follows mannitol treatment).

4.6 Fertility, pregnancy and lactation

Fertility
Animal reproduction studies have not been conducted with mannitol. It is also not known whether mannitol can affect reproduction capacity.

Use in pregnancy (Category B2)
Teratogenic effects: Animal reproduction studies have not been conducted with mannitol. It is also not known whether mannitol can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity. Mannitol should be given to a pregnant woman only if clearly needed.

Use in lactation
It is not known whether this medicine is excreted in human milk. Because many medicines are excreted in human milk, caution should be exercised when mannitol is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Extensive use of mannitol over the last several decades has produced recorded adverse events, in a variety of clinical settings that are isolated or idiosyncratic in nature. None of these adverse reactions have occurred with any great frequency or with any security in attributing them to mannitol.

The inability to clearly exclude the medicine related nature of such events in these isolated reports prompts the necessity to list the reactions that have been observed in patients during the following mannitol infusions.

Immediate reactions: can be noted, very rarely and in the same manner than with all Osmitrol solutions. (In these cases the infusion must be discontinued).

Gastrointestinal Disorder	Nausea Vomiting
Hypersensitivity reactions	Local pain Skin necrosis Thrombophlebitis at the site if Intravenous Infusion Rhinitis Angio-oedema Allergic reaction Anaphylactic shock
Neurological reactions	Chills Dizziness Urticaria Fever Headache Blurred vision Intracranial pressure increase
Circulatory effects	Hypotension Hypertension Tachycardia Cardiac arrhythmia Angina-like chest pain Pulmonary congestion oedema Convulsions Congestive cardiac failure
Renal effects	Nephrosis osmotic Alveolar nephrosis Large doses of mannitol have been known to cause acute renal failure even in patients with satisfactory pre-treatment renal function Excessive diuresis Urinary retention
Blood disturbances	Acidosis Fluid and Electrolyte imbalance

Metabolic/Nutritional disorder	Dehydration Oedema Cramps Thirst Dryness of mouth

Of far greater clinical significance are a variety of events that are related to inappropriate recognition and monitoring of fluid shifts. These are not intrinsic adverse reactions to the medicine but the consequence of manipulating osmolarity by an agency in a therapeutically inappropriate manner. Failure to recognise severe impairment of renal function with the high likelihood of non-diuretic response can lead to aggravated dehydration of tissues and increased vascular fluid load. Induced diuresis in the presence of pre-existing haemoconcentration and pre-existing deficiency of water and electrolytes can lead to serious imbalances. Expansion of the extracellular space can aggravate cardiac decompensation or induce it in the presence of latent heart failure. Pulmonary congestion or oedema can be seriously aggravated with the expansion of the extracellular fluid space by osmotic shift of water can induce or aggravate pre-existing hyponatraemia.

These are not truly adverse reactions to the medicine and can be appropriately prevented by evaluation of degree of renal failure with a test dose response to mannitol when indicated; evaluation of hypervolaemia and hypovolaemia; sodium and potassium levels; haemodilution or haemoconcentration and evaluation of renal, cardiac and pulmonary function at the onset of therapy.

The following adverse reactions have been reported in the post-marketing experience listed by MedDRA System Organ Class (SOC):

Immune system disorders: Anaphylactic/anaphylactoid reactions, including anaphylaxis, with skin, gastrointestinal, and severe circulatory (hypotension), and respiratory manifestations (e.g. dyspnoea). Other hypersensitivity/infusion reactions include hypertension, pyrexia, chills, sweating, cough, musculoskeletal stiffness and myalgia, urticaria/rash, pruritus, generalised pain, discomfort, nausea, vomiting, and headache.

Metabolism and nutrition disorders: Fluid and electrolyte imbalances, including hypervolaemia, peripheral oedema, dehydration, hyponatraemia, hypernatraemia, hyperkalaemia, hypokalaemia; metabolic acidosis, metabolic alkalosis.

Nervous system disorders: CNS toxicity manifested by, e.g. coma, convulsion, confusion, lethargy, rebound increase in intracranial pressure, dizziness.

Cardiac disorders: Congestive cardiac failure, palpitations.

Respiratory, thoracic and mediastinal disorders: Pulmonary oedema.

Gastrointestinal disorders: Thirst, dry mouth.

Renal and urinary disorders: Renal failure acute, osmotic nephrosis, renal impairment, azotemia, anuria, haematuria, oliguria, polyuria.

General disorders and administration site conditions: Asthenia, malaise; infusion site reactions, including infusion site phlebitis, infusion site inflammation, infusion site pain, infusion site rash, infusion site erythema, infusion site pruritus; compartment syndrome, bullous eruptions, and swelling at the injection site associated with extravasation (see section 4.4/ Infusion site reactions).

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 https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose
In case of suspected overdose, treatment with Osmitrol should be stopped immediately.

Prolonged administration or rapid infusion of large volumes of hyperosmotic solutions may result in circulatory overload and acidosis. Headache, nausea and shivering without temperature change may represent initial signs/symptoms. Confusion, lethargy, convulsions, stupor and coma may follow.

Signs and symptoms of overdose with mannitol may include acute renal failure, electrolytes imbalance, hypervolaemia and CNS toxicity.

Management is symptomatic and supportive, with monitoring of fluid electrolyte balance. Mannitol is dialyzable; haemodialysis may be useful in eliminating mannitol.

For advice on the management of overdose please contact the National Poisons Centre on phone number: 0800 764 766 [0800 POISON] in New Zealand (or 131126 in Australia).

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Solutions producing osmotic diuresis.
ATC code: B05BC01

General
Osmitrol infusion solution (mannitol intravenous infusion, BP) is a sterile, nonpyrogenic solution of mannitol BP, in a single dose container for intravenous administration. Mannitol $C_6H_{14}O_6$ is a six carbon sugar alcohol prepared commercially by the reduction of glucose. The molecular weight for mannitol is 182.2, CAS Number 69-65-8. Although virtually inert metabolically in humans, it occurs naturally in fruits and vegetables. Mannitol is an obligatory osmotic diuretic. The pH is adjusted with sodium hydroxide and hydrochloric acid. Composition, osmolarity and pH are shown in the following table.

	Size	*Composition (mannitol BP)*	**Osmolality mOsmol/kg*	*pH*
10% Osmitrol infusion solution (10% mannitol IV infusion BP)	1000mL	100g/1000mL	596	5.5 (4.5 to 7.0)
20% Osmitrol infusion solution (20% mannitol IV infusion BP)	500mL	100g/500mL	1192	5.0 (4.5 to 7.0)
*	An injection with an osmolalaity within the range of 250 to 350mOsm/kg is considered to be isotonic. Administration of substantially hypertonic solutions may cause vein damage.			

The VIAFLEX plastic container is fabricated from a specially formulated polyvinyl chloride (PL 146 Plastic). The amount of water that can permeate from inside the container into the overwrap is insufficient to affect the solution significantly. Solutions in contact with the plastic container can leach out certain of its chemical components in very small amounts within the expiration period, e.g. di-2-ethylhexyl phthalate (DEHP), up to 5 parts per million. However, the safety of the plastic has

been confirmed in tests in animals according to USP biological tests for plastic containers as well as tissue culture toxicity studies.

Pharmacology
Osmitrol infusion solution (mannitol intravenous infusion, BP) is one of the non-electrolyte, obligatory, osmotic diuretics. It is freely filterable at the renal glomerulus, is poorly reabsorbed by the renal tubule, is not secreted by the tubule, and is pharmacologically inert.

Mannitol, when administered intravenously, exerts its osmotic effect as a solute of relatively small molecular size being largely confined to the extracellular space. Only relatively small amounts of the dose administered are metabolised. Mannitol is readily diffused through the glomerulus of the kidney over a wide range of normal and impaired kidney function. In this fashion, approximately 80% of a 100 gram dose of mannitol will appear in the urine in three hours with lesser amounts thereafter. Even at peak concentrations, mannitol will exhibit less than 10% of tubular reabsorption and is not secreted by the tubular cells. Mannitol will hinder tubular reabsorption of water and enhance excretion of sodium and chloride by elevating the osmolarity of the glomerular filtrate.

The increase in extracellular osmolarity affected by the intravenous administration of mannitol will induce the movement of intracellular water to the extracellular and vascular spaces. The action underlies the role of mannitol in reducing intracranial pressure, intracranial oedema, and reducing elevated intraocular pressure.

5.2 Pharmacokinetic properties
When administered intravenously, mannitol is eliminated largely unmetabolised through the glomeruli. It is freely filtered by the glomeruli, with less than 10% tubular reabsorption and is not secreted by tubular cells. The elimination half-life in adults is approximately 2 hours, longer where renal failure is present. 80% of an intravenous dose is excreted unchanged within 3 hours.

5.3 Preclinical safety data
The preclinical safety assessment of mannitol 10% or 20% in animals is not relevant as mannitol is a substance with well-established use in patients and is covered by appropriate pharmacopoeial references.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Osmitrol 10%	Water for injections.
Osmitrol 20%	Water for injections.

6.2 Incompatibilities
Incompatibility with blood
Electrolyte and mannitol intravenous infusions should be not given co-jointly with blood. If it is essential that blood be given simultaneously, at least 20mEq of sodium chloride should be added to each litre of mannitol solution to avoid pseudoagglutination.

Incompatibility with additives
There may be potential incompatibility with additives which include the risk of precipitation if potassium or sodium chloride is added to mannitol. Also some antibiotics including cefepime, imipenem or cilastatin may be incompatible with mannitol.

6.3 Shelf life
24 months as packaged for sale in Viaflex bag.

6.4 Special precautions for storage

Store at or below +30°C.

Exposure of pharmaceutical products to heat should be minimised. Avoid excessive heat. It is recommended the product should be stored below 30°C; brief exposure up to 40°C does not adversely affect the product.

6.5 Nature and contents of container

Not all pack sizes and presentations may be marketed.

Osmitrol infusion solution (mannitol intravenous infusion, BP) in Viaflex plastic containers is available as follows:

Product Name	*Size (mL)*	*Code*
10% Osmitrol infusion solution (10% mannitol IV infusion BP)	1000mL	AHB3026
20% Osmitrol infusion solution (20% mannitol IV infusion BP)	500mL	AHB3025

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements. The product is for single use in one patient only. Discard any residue immediately after use. Do not use if container is damaged or if solution is not clear.

7 MEDICINE SCHEDULE

General Sale Medicine.

8 SPONSOR

Osmitrol solution for infusion is distributed in New Zealand by:

Baxter Healthcare Ltd
33 Vestey Drive
Mt Wellington
Auckland 1060.

Baxter Healthcare Ltd
PO Box 14 062
Panmure
Auckland 1741

Phone (09) 574 2400.

Osmitrol solution for infusion is distributed in Australia by:
Baxter Healthcare Pty Ltd
1 Baxter Drive
Old Toongabbie, NSW 2146.

9 DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine:

Osmitrol 10% 24 September 1981.
Osmitrol 20% 24 September 1981.

10 DATE OF REVISION OF THE TEXT

5 October 2017.

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All sections	Document reformatted to SPC format.
4.4	*Crystallisation* Inclusion of following sentence: "…The recommended method is to use dry heat e.g. warming pad."
10	Date of revision of text, and footer updated.

Based on Australian PI latest amendment 7 December 2015; and CCSI4322015Aug20.

Please refer to the Medsafe website (www.medsafe.govt.nz) for most recent data sheet.

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