

New Zealand Data Sheet

1. PRODUCT NAME

MEROPENEM RANBAXY 500 mg powder for injection
MEROPENEM RANBAXY 1 g powder for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each MEROPENEM RANBAXY 500 mg vial contains meropenem trihydrate equivalent to 500 mg anhydrous meropenem.

Each MEROPENEM RANBAXY 1 g vial contains meropenem trihydrate equivalent to 1 g anhydrous meropenem.

Excipient(s) with known effect

Each MEROPENEM RANBAXY 500 mg vial contains 104 mg sodium carbonate.
Each MEROPENEM RANBAXY 1 g vial contains 208 mg sodium carbonate.
For the full list of excipients, *see Section 6.1.*

3. PHARMACEUTICAL FORM

White to pale yellow crystalline sterile powder packed in clear Type 1 glass vials for reconstitution for injection or infusion.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

MEROPENEM RANBAXY is indicated for treatment, in adults and children aged 3 months and older, of the following infections caused by single or multiple susceptible bacteria (*see Section 5.1*) and as empiric therapy prior to the identification of the causative organisms:

- Lower Respiratory Tract Infections
- Urinary Tract Infections, including complicated infections
- Intra-abdominal Infections
- Gynaecological Infections, including postpartum infections
- Skin and Skin Structure Infections
- Meningitis
- Septicaemia
- Empiric treatment, including initial monotherapy, for presumed bacterial infections in host-compromised, neutropenic patients.

Because of its broad spectrum of bactericidal activity against Gram-positive and Gram-negative aerobic and anaerobic bacteria, meropenem is effective for the treatment of polymicrobial infections.

4.2. Dose and method of administration

Dose

Adults

500 mg to 1 g by intravenous administration every 8 hours depending on type and severity of infection, the known or expected susceptibility of the pathogen(s) and the condition of the patient.

Exceptions

1. Febrile episodes in neutropenic patients - the dose should be 1 g every 8 hours.
2. Meningitis - the dose should be 2 g every 8 hours.

As with other antibiotics, caution may be required in using meropenem as monotherapy in critically ill patients with known or suspected *Pseudomonas aeruginosa* lower respiratory tract infection.

Regular sensitivity testing is recommended when treating *Pseudomonas aeruginosa* infection.

Special populations

Adults with impaired renal function

Dosage should be reduced in adult patients with creatinine clearance less than 51 mL/min, as scheduled below:

Creatinine Clearance (mL/min)	Dose (based on unit doses of 500 mg, 1 g, 2 g every 8 hours)	Frequency
26 to 50	one unit dose	every 12 hours
10 to 25	one-half unit dose	every 12 hours
<10	one-half unit dose	every 24 hours

Meropenem is cleared by haemodialysis. If continued treatment with MEROPENEM RANBAXY for Injection is necessary, the unit dose (based on the type and severity of infection) is recommended at the completion of the haemodialysis procedure to re-institute effective treatment.

There is no experience with peritoneal dialysis.

Adults with hepatic insufficiency

No dosage adjustment is necessary in patients with impaired hepatic metabolism.

Elderly Patients

No dosage adjustment is required for the elderly with normal renal function or creatinine clearance values above 50 mL/min.

Paediatric population

Children under 3 months of age

Efficacy and tolerability in infants under 3 months of age have not been established; therefore, meropenem is not recommended for use below this age.

Children over 3 months and up to 12 years of age and up to 50 kg body weight

The recommended intravenous dose is 10 to 40 mg/kg every 8 hours depending on type and severity of infection, the known or suspected susceptibility of the pathogen(s) and the condition of the patient.

Exceptions

1. Febrile episodes in neutropenic patients - the dose should be 20 mg/kg every 8 hours.
2. Meningitis - the dose should be 40 mg/kg every 8 hours.

Children over 50 kg body weight

The adult dosage should be used.

Children with impaired renal function

There is no experience in children with renal impairment.

Method of Administration

MEROPENEM RANBAXY for Injection should be given as an intravenous bolus injection over approximately 5 minutes or by intravenous infusion over approximately 15 to 30 minutes (*see Sections 6.2, 6.3 and 6.6*). There is limited safety data available to support the administration of a 2 g bolus dose in adults and the administration of a 40 mg/kg bolus dose in children.

For instructions on reconstitution of the medicinal product before administration, *see Section 6.6*.

4.3. Contraindications

MEROPENEM RANBAXY for Injection is contraindicated in patients who have demonstrated hypersensitivity reactions to meropenem, or other carbapenems, penicillins or other β -lactam antibiotics.

4.4. Special warnings and precautions for use

Hypersensitivity reaction (allergic/anaphylaxis)

Serious and occasionally fatal hypersensitivity reactions have been reported in patients receiving therapy with β -lactams (see Sections 4.3 and 4.8). These reactions are more likely to occur in persons with a history of sensitivity to multiple allergens. There have been reports of patients with a history of penicillin hypersensitivity who have experienced severe hypersensitivity when treated with another β -lactam. Before initiating treatment with meropenem, careful inquiry should be made concerning previous hypersensitivity reactions to carbapenems, penicillins, or other β -lactam antibiotics. If an allergic reaction to meropenem occurs discontinue the drug. Serious hypersensitivity reactions may require adrenaline and other emergency measures.

***Pseudomonas aeruginosa* resistance**

As with other β -lactam antibiotics, strains of *Pseudomonas aeruginosa* may develop resistance on treatment with meropenem. Development of resistance has been reported in pseudomonal hospital acquired lower respiratory tract infections. In such cases, meropenem should be used with caution and repeat sensitivity testing is recommended.

Gastrointestinal disease

History of colitis

Antibiotics should be prescribed with care for individuals with a history of gastrointestinal disease, especially ulcerative colitis, regional enteritis, or antibiotic associated colitis (see Section 4.8).

Pseudomembranous colitis

Pseudomembranous colitis has been observed with practically all antibiotics and may vary in severity from slight to life-threatening. It is important to consider the diagnosis of pseudomembranous colitis in the case of patients who develop diarrhoea when using an antibiotic. Although studies indicate that a toxin produced by *Clostridium difficile* is one of the main causes of antibiotic-associated colitis, other causes should be considered.

Mild cases usually respond to drug discontinuation alone. However, in moderate to severe cases appropriate therapy such as oral antibacterial agents effective against *Clostridium difficile* should be considered. Fluids, electrolytes and protein replacement should be provided when indicated.

Drugs that delay peristalsis, e.g. opiates and diphenoxylate with atropine, may prolong and/or worsen the condition and should not be used.

Seizures

Seizures have infrequently been reported during treatment with carbapenems, including meropenem, *see Section 4.8*.

Controlled sodium diet

This medicinal product contains sodium which should be taken into consideration for patients on a controlled sodium diet.

Use in severe meningitis

Neurological sequelae were reported following treatment of severe meningitis with meropenem. In clinical trials these adverse events were reported in 23 of 148 patients treated with meropenem and in 17 of 144 patients treated with comparator antibiotics.

Use in patients with liver disease

Hepatic function should be closely monitored during treatment with meropenem due to the risk of hepatic toxicity (hepatic dysfunction with cholestasis and cytolysis). Patients with pre-existing liver disorders should have liver function monitored during treatment with meropenem.

Use with valproic acid/sodium valproate

The concomitant use of valproic acid/sodium valproate and meropenem is not recommended, *see Section 4.5*.

Interference with serological testing

A positive direct or an indirect Coombs' test may develop.

4.5. Interaction with other medicines and other forms of interaction

Meropenem has been administered concomitantly with many other medications without apparent adverse interaction. However, no specific medicine interaction studies other than with probenecid were conducted.

Probenecid

Probenecid competes with meropenem for active tubular secretion and thus inhibits the renal excretion of meropenem with the effect of increasing the elimination half-life and plasma concentration of meropenem. As the potency and duration of action of meropenem dosed without probenecid are adequate the co-administration of probenecid with meropenem is not recommended. The potential effect of meropenem on the protein binding of other drugs or metabolism has not been studied. However, the protein binding is so low (approximately 2%)

that no interactions with other compounds would be expected on the basis of this mechanism.

Valproic acid/sodium valproate

A clinically significant reduction in serum valproic acid concentration has been reported in patients receiving carbapenem antibiotics resulting a 60-100% decrease valproic acid levels in about two days. Due to the rapid onset and the extent of the decrease, co-administration of MEROPENEM RANBAXY for Injection in patients stabilised on valproic acid/sodium valproate is not considered to be manageable and therefore should be avoided, *see Section 4.4*.

The concomitant use of meropenem and valproic acid/sodium valproate/valpromide is not recommended.

Oral anticoagulants

Simultaneous administration of antibiotics with warfarin may augment its anticoagulant effects. There have been many reports of increases in the anticoagulant effects of orally administered anticoagulant agents, including warfarin, in patients who are concomitantly receiving antibacterial agents. The risk may vary with the underlying infection, age and general status of the patient so that the contribution of the antibiotic to the increase in INR (international normalized ratio) is difficult to assess. It is recommended that the INR should be monitored frequently during and shortly after co-administration of antibiotics with an oral anticoagulant agent.

4.6. Fertility, pregnancy and lactation

Pregnancy

There are no adequate or well controlled trials of meropenem in pregnant women. Reproduction studies conducted with meropenem in rats have shown no embryotoxicity or teratogenicity, *see Section 5.3*.

Because reproduction studies are not always predictive of human response, MEROPENEM RANBAXY for Injection should not be used in pregnancy unless the potential benefit justifies the potential risk to the foetus.

Breast-feeding

Meropenem has been reported to be excreted in human breast milk. MEROPENEM RANBAXY for Injection should not be used in breast-feeding women unless the potential benefit justifies the potential risk to the baby.

Fertility

Fertility was not impaired in rats with exposures based on the area under the curve (AUC) slightly greater than those observed in patients at the recommended intravenous dose.

4.7. Effects on ability to drive and use machines

No studies on the ability to drive and use machines have been performed. However, when driving or operating machines it should be taken into account that headache, paraesthesiae and convulsions have been reported for meropenem, *see Section 4.8*.

4.8. Undesirable effects

Tabulated risk of adverse reactions

Meropenem is generally well tolerated. In clinical trials, adverse events lead to cessation of treatment in less than 1% of patients. Serious adverse events are rare.

In the table below all adverse reactions are listed by system organ class and frequency: very common ($\geq 1/10$); common ($\geq 1/100$ to $<1/10$); uncommon ($\geq 1/1,000$ to $<1/100$); rare ($\geq 1/10,000$ to $<1/1,000$); very rare ($< 1/10,000$); not known (cannot be estimated from the available data).

System Organ Class	Frequency	Event
Infections and infestations	Uncommon	Oral and vaginal candidiasis
Blood and lymphatic system disorders	Common	Reversible thrombocythaemia
	Uncommon	Eosinophilia, leucopenia, thrombocytopenia, neutropenia
	Rare	Agranulocytosis
	Very rare	Haemolytic anaemia
Immune system disorders	Uncommon	Systemic allergic reactions (hypersensitivity) may occur following administration of meropenem. These reactions may include angioedema and manifestations of anaphylaxis
Nervous system disorders	Common	Headache
	Uncommon	Paraesthesia
	Rare	Convulsions
Gastrointestinal disorders	Common	Nausea, vomiting, diarrhoea, abdominal pain
	Uncommon	Pseudomembranous colitis, antibiotic-associated colitis.
Hepatobiliary disorders	Common	Reversible increases in serum transaminases (alanine aminotransferase, aspartate aminotransferase), gammaglutamyltransferase, bilirubin, alkaline phosphatase and lactic dehydrogenase alone or in combination have been reported
Skin and subcutaneous tissue disorders	Common	Rash, pruritus
	Uncommon	Urticaria, erythema multiforme, Stevens- Johnson Syndrome, toxic epidermal necrolysis
	Not known	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS Syndrome)
General disorders and administration site conditions	Common	Inflammation, thrombophlebitis, and pain at the injection site

Other

Nervous system disorders

Delirium, and hallucinations have been reported but a causal link with meropenem has not been established.

Cardiac disorders

Cardiac failure has been reported but a causal link with meropenem has not been established.

Respiratory, thoracic and mediastinal disorders

Pneumonia and respiratory failure have been reported but a causal link with meropenem has not been established.

Hepatobiliary disorders

Jaundice and hepatic failure have been reported but a causal link with meropenem has not been established.

General disorders and administration site conditions

Fever and septicaemia have been reported but a causal link with meropenem has not been established.

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 reactions <https://nzphvc.otago.ac.nz/reporting/>

4.9. Overdose

The pharmacological properties and mode of administration make it unlikely that intentional overdose will occur. Accidental overdosage could occur during therapy, particularly in patients with renal impairment. Treatment of overdosage should be symptomatic. In normal individuals rapid renal elimination will occur. In subjects with renal impairment haemodialysis will remove meropenem and its metabolite.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: ANTIINFECTIVES FOR SYSTEMIC USE- Carbapenems; ATC code: J01DH02

Mechanism of Action

Meropenem is a carbapenem antibiotic for parenteral use, that is stable to human dehydropeptidase-1 (DHP-1).

Meropenem exerts its bactericidal action by interfering with vital bacterial cell wall synthesis. The ease with which it penetrates bacterial cell walls, its high level of stability to all serine β -lactamases and its marked affinity for the Penicillin Binding Proteins (PBPs) explain the potent bactericidal action of meropenem against a broad spectrum of aerobic and anaerobic bacteria. Bactericidal concentrations are commonly the same as the minimum inhibitory concentrations (MICs).

Meropenem is stable in susceptibility tests and these tests can be performed using normal routine methods. In vitro tests show that meropenem acts synergistically with various antibiotics. It has been demonstrated both *in vitro* and *in vivo* that meropenem has a post-antibiotic effect against Gram-positive and Gram-negative organisms.

Mechanism of resistance

Bacterial resistance to meropenem may result from: (1) decreased permeability of the outer membrane of Gram-negative bacteria (due to diminished production of porins) (2) reduced affinity of the target PBPs (3) increased expression of efflux pump components, and (4) production of β -lactamases that can hydrolyse carbapenems.

Localised cluster of infections due to carbapenem-resistant bacteria have been reported in some regions.

The susceptibility to meropenem of a given clinical isolate should be determined by standard methods. Interpretations of test results should be made in accordance with local infectious diseases and clinical microbiology guidelines.

The antibacterial spectrum of meropenem includes the following species, based on clinical experience and therapeutic guidelines.

Commonly susceptible species: Gram-positive aerobes

Enterococcus faecalis (note that *E. faecalis* can naturally display intermediate susceptibility), *Staphylococcus aureus* (methicillin-susceptible strains only: methicillin-resistant staphylococci including MRSA are resistant to meropenem), *Staphylococcus* species including *Staphylococcus epidermidis* (methicillin-susceptible strains only: methicillin-resistant staphylococci including MRSE are resistant to meropenem), *Streptococcus agalactiae* (Group B streptococcus), *Streptococcus milleri* group (*S. anginosus*, *S. constellatus*, and *S. intermedius*), *Streptococcus pneumoniae*, *Streptococcus pyogenes* (Group A streptococcus).

Commonly susceptible species: Gram-negative aerobes

Citrobacter freundii, *Citrobacter koseri*, *Enterobacter aerogenes*, *Enterobacter cloacae*,

Escherichia coli, *Haemophilus influenzae*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Morganella morganii*, *Neisseria meningitidis*, *Proteus mirabilis*, *Proteus vulgaris*, *Serratia marcescens*.

Commonly susceptible species: Gram-positive anaerobes

Clostridium perfringens, *Peptoniphilus asaccharolyticus*, *Peptostreptococcus* species (including *P. micros*, *P. anaerobius*, *P. magnus*).

Commonly susceptible species: Gram-negative anaerobes

Bacteroides caccae, *Bacteroides fragilis* group, *Prevotella bivia*, *Prevotella disiens*.

Species for which acquired resistance may be a problem: Gram-positive aerobes
Enterococcus faecium (*E. faecium* can naturally display intermediate susceptibility even without acquired resistance mechanisms; note that in some European countries the frequency of resistance among *E. faecium* is greater than 50 % of isolates).

Species for which acquired resistance may be a problem: Gram-negative aerobes

Acinetobacter species, *Burkholderia cepacia*, *Pseudomonas aeruginosa*.

Inherently resistant organisms: Gram-negative aerobes

Stenotrophomonas maltophilia, *Legionella* species.

Other inherently resistant organisms

Chlamydophila pneumoniae, *Chlamydophila psittaci*, *Coxiella burnetii*, *Mycoplasma pneumoniae*.

The published medical microbiology literature describes *in vitro* meropenem-susceptibilities of many other bacterial species. However the clinical significance of such *in vitro* findings is uncertain. Advice on the clinical significance of *in vitro* findings should be obtained from local infectious diseases and clinical microbiology experts and local professional guidelines. meropenem and imipenem have a similar profile of clinical utility and activity against multiresistant bacteria. However, meropenem is intrinsically more potent against *Pseudomonas aeruginosa* and may be active *in vitro* against imipenem-resistant strains. Meropenem is active *in vitro* against many strains resistant to other b-lactam antibiotics. This is explained in part by enhanced stability to b-lactamases. Activity *in vitro* against strains resistant to unrelated classes of antibiotics such as aminoglycosides or quinolones is common. The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

5.2. Pharmacokinetic properties

In healthy subjects the mean plasma half-life is approximately 1 hour; the mean volume of distribution is approximately 0.25 L/kg (11-27 L) and the mean clearance is 287 mL/min at 250 mg falling to 205 mL/min at 2 g. Doses of 500, 1000 and 2000 mg doses infused over 30 minutes give mean C_{max} values of approximately 23, 49 and 115 µg/mL respectively, corresponding AUC values were 39.3, 62.3 and 153 µg.h/mL. After infusion over 5 minutes C_{max} values are 52 and 112 µg/mL after 500 and 1000 mg doses respectively. When multiple doses are administered 8-hourly to subjects with normal renal function, accumulation of meropenem does not occur. A study of 12 patients administered meropenem 1000 mg 8 hourly post-surgically for intraabdominal infections showed a comparable C_{max} and half-life to normal subjects but a greater volume of distribution 27 L.

Intravenous infusions of 1g over 2 minutes, 3 minutes and 5 minutes were compared in a three-way crossover trial. These durations of infusion resulted in peak plasma levels of 110, 91 and 94 microgram/mL respectively.

Distribution

The average plasma protein binding of meropenem was approximately 2% and was independent of concentration. Meropenem has been shown to penetrate well into several body fluids and tissues: including lung, bronchial secretions, bile, cerebrospinal fluid, gynaecological tissues, skin, fascia, muscle, and peritoneal exudates.

Metabolism

Meropenem is metabolised by hydrolysis of the b-lactam ring generating a microbiologically inactive metabolite. In vitro meropenem shows reduced susceptibility to hydrolysis by human dehydropeptidase-I (DHP-I) compared to imipenem and there is no requirement to co-administer a DHP-I inhibitor.

Elimination

Meropenem is primarily excreted unchanged by the kidneys; approximately 70 % (50 –75 %) of the dose is excreted unchanged within 12 hours. A further 28% is recovered as the microbiologically inactive metabolite. Faecal elimination represents only approximately 2% of the dose. The measured renal clearance and the effect of probenecid show that meropenem undergoes both filtration and tubular secretion.

Special populations

Renal insufficiency

Renal impairment results in higher plasma AUC and longer half-life for meropenem. There were AUC increases of 2.4 fold in patients with moderate impairment (CrCL 33-74 mL/min), 5 fold in severe impairment (CrCL 4-23 mL/min) and 10 fold in haemodialysis patients (CrCL <2 mL/min) when compared to healthy subjects (CrCL >80 mL/min). The AUC of the microbiologically inactive ring opened metabolite was also considerably increased in patients with renal

impairment. Dose adjustment is recommended for patients with moderate and severe renal impairment (*see section 4.2*).

Meropenem is cleared by haemodialysis with clearance during haemodialysis being approximately 4 times higher than in anuric patients.

Hepatic insufficiency

A study in patients with alcoholic cirrhosis shows no effect of liver disease on the pharmacokinetics of meropenem after repeated doses.

Adult patients

Pharmacokinetic studies performed in patients have not shown significant pharmacokinetic differences versus healthy subjects with equivalent renal function. A population model developed from data in 79 patients with intra-abdominal infection or pneumonia, showed a dependence of the central volume on weight and the clearance on creatinine clearance and age.

Elderly

Pharmacokinetic studies in healthy elderly subjects (65-80 years) have shown a reduction in plasma clearance, which correlated with age-associated reduction in creatinine clearance, and a smaller reduction in non-renal clearance. No dose adjustment is required in elderly patients, except in cases of moderate to severe renal impairment (*see section 4.2*).

Paediatric population

The pharmacokinetics in infants and children with infection at doses of 10, 20 and 40 mg/kg showed C_{max} values approximating to those in adults following 500, 1000 and 2000 mg doses, respectively. Comparison showed consistent pharmacokinetics between the doses and half-lives similar to those observed in adults in all but the youngest subjects (<6 months t_{1/2} 1.6 hours). The mean meropenem clearance values were 5.8 mL/min/kg (6-12 years), 6.2 mL/min/kg (2-5 years), 5.3 mL/min/kg (6-23 months) and 4.3 mL/min/kg (2-5 months). Approximately 60% of the dose is excreted in urine over 12 hours as meropenem with a further 12% as metabolite. Meropenem concentrations in the CSF of children with meningitis are approximately 20% of concurrent plasma levels although there is significant inter-individual variability.

The pharmacokinetics of meropenem in neonates requiring anti-infective treatment showed greater clearance in neonates with higher chronological or gestational age with an overall average half-life of 2.9 hours. Monte Carlo simulation based on a population PK model showed that a dose regimen of 20 mg/kg 8 hourly achieved 60%T>MIC for *P. aeruginosa* in 95% of pre-term and 91% of full term neonates.

5.3. Preclinical safety data

Animal studies indicate that meropenem is well tolerated by the kidney. Histological evidence of renal tubular damage was seen in mice and dogs only at doses of 2000 mg/kg and above.

Meropenem is generally well tolerated by the CNS. Effects were seen only at very high doses of 2000 mg/kg and above.

The IV LD50 of meropenem in rodents is greater than 2000 mg/kg. In repeat dose studies of up to 6 months duration only minor effects were seen including a small decrease in red cell parameters and an increase in liver weight in dogs at 500 mg/kg.

There was no evidence of mutagenic potential in the 5 tests conducted and no evidence of reproductive toxicity including teratogenic potential in studies at the highest possible level in rats and monkeys. (The no effect dose level of a small reduction in F1 body weight in rats was 120 mg/kg).

There was increased evidence of abortions at 500 mg/kg in a preliminary study in monkeys. There was no evidence of increased sensitivity to meropenem in juveniles compared to adult animals. The intravenous formulation was well tolerated in animal studies.

The intramuscular formulation caused reversible injection site necrosis.

The sole metabolite of meropenem had a similar low profile of toxicity in animal studies.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Anhydrous sodium carbonate

6.2. Incompatibilities

MEROPENEM RANBAXY is compatible with the infusion solutions listed in section 6.6 and should not be mixed with or physically added to solutions containing other drugs.

6.3. Shelf life

24 months from date of manufacture.

After reconstitution:

To reduce microbiological hazard, solutions of MEROPENEM RANBAXY for Injection should be used as soon as practicable after reconstitution. If storage is necessary, refer to the table below for guidance.

Diluent	Hours stable	
	up to 25°C	4°C
Vials constituted with Water for Injection for bolus injection	8	24
Solutions (1 to 20 mg/mL) prepared with:		
0.9% sodium chloride	8	48
5% glucose	3	14
5% glucose and 0.225% sodium chloride	3	14
5% glucose and 0.9% sodium chloride	3	14
5% glucose and 0.15% potassium chloride	3	14
2.5% or 10% mannitol intravenous infusion	3	14
normosol-M in 5% glucose intravenous infusion	3	14
10% glucose	2	8
5% glucose and 0.02% sodium bicarbonate intravenous infusion	2	8

6.4. Special precautions for storage

Store at or below 25°C.

Do not freeze the reconstituted solution.

6.5. Nature and contents of container

White to pale yellow crystalline sterile powder in a Type 1 glass vial with a grey rubber stopper and an aluminium seal.

MEROPENEM RANBAXY for Injection is available in pack sizes of 1, 5 or 10 vials.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

Bolus intravenous injection

MEROPENEM RANBAXY for Injection to be used for bolus intravenous injection should be constituted with sterile Water for Injection (10 mL per 500 mg meropenem). This provides an approximate available concentration of 50 mg/mL. Reconstituted solutions are both clear and colourless to pale yellow.

Intravenous infusion

MEROPENEM RANBAXY for Injection to be used for intravenous infusion may be directly

reconstituted with a compatible infusion fluid and then further diluted (50 to 200 mL) with the compatible infusion fluid.

Compatible infusion fluids

MEROPENEM RANBAXY for Injection is compatible with the following infusion fluids:

- 0.9% sodium chloride intravenous infusion
- 5% or 10% glucose intravenous infusion
- 5% glucose intravenous infusion with 0.02% sodium bicarbonate
- 5% glucose and 0.9% sodium chloride intravenous infusion
- 5% glucose with 0.225% sodium chloride intravenous infusion
- 5% glucose with 0.15% potassium chloride intravenous infusion
- 2.5% and 10% mannitol intravenous infusion
- normosol-M in 5% glucose intravenous infusion.

Displacement values

500 mg vial: 0.4 mL

1 g vial: 0.9 mL

Standard aseptic technique should be employed during constitution and administration.

Shake reconstituted solution before use.

All vials are for single use in one patient only. Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription medicine.

8. SPONSOR

Douglas Pharmaceuticals Ltd

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9. DATE OF FIRST APPROVAL

09 February 2012

10.DATE OF REVISION OF THE TEXT

11 January 2018

Summary table of changes

Section Changed	Summary of new information
All	Revised to reflect SPC format
4.4, 4.5, 4.6, 4.8	Information in line with Source document
4.8	Added DRESS as an adverse reaction