

NEW ZEALAND DATA SHEET

Meropenem Sandoz[®]

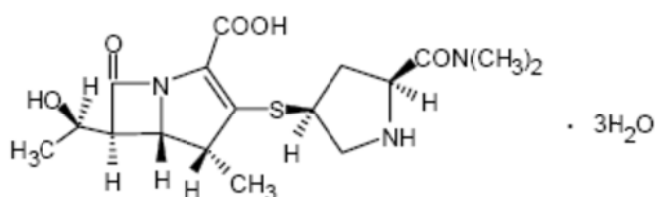
Meropenem trihydrate, 500mg, 1g powder for injection

Name of the Medicine

Active Ingredient: Meropenem trihydrate

Chemical name: (4R,5S,6S)-3-[[[(3S,5S)-5-(Dimethylcarbamoyl)-3-pyrrolidiny]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-carboxylic acid, trihydrate

Chemical structure:



CAS Number: 119478-56-7

Empirical formula: C₁₇H₂₅N₃O₅S·3H₂O MW: 437.52

Presentation

Meropenem Sandoz powder for intravenous injection or infusion is presented as a sterile white to pale yellow crystalline powder containing meropenem trihydrate equivalent to meropenem, 500mg or 1g, blended with sodium carbonate anhydrous. Meropenem Sandoz contains 208mg sodium carbonate anhydrous for each gram of meropenem.

Meropenem Sandoz	500mg	1g
<i>Active ingredient</i>		
Meropenem (as trihydrate)	571mg	1.14g
Equivalent to meropenem	500mg	1g
<i>Excipient</i>		
Sodium carbonate anhydrous	104mg	208mg

Pharmacology

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

Pharmacodynamics

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 most serine β-lactamases and its high affinity for the Penicillin Binding Proteins (PBPS) explain the potent bactericidal action of meropenem against a broad spectrum of aerobic and anaerobic bacteria. The bactericidal concentrations are generally within one doubling dilution of the minimum inhibitory concentrations

(MICs).

Meropenem is stable in susceptibility tests and these tests can be performed using the normal routine systems. *In vitro* tests show that meropenem can act 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 multi resistance 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 β -lactam antibiotics. This is explained in part by enhanced stability to β -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.

Pharmacokinetics

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 μ g/mL respectively, corresponding AUC values were 39.3, 62.3 and 153 μ g.h/mL. After infusion over 5 minutes C_{max} values are 52 and 112 μ g/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 intra-abdominal infections showed a comparable C_{max} and half-life to normal subjects but a greater volume of distribution 27 L.

Intravenous infusions of 1 g 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 β -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.

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 Dosage and administration).

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.

Paediatrics

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 2000mg 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.

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 Dosage And Administration).

Indications

Meropenem Sandoz is indicated for treatment, in adults and children, of the following infections caused by single or multiple susceptible bacteria 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 Sandoz is effective for the treatment of polymicrobial infections.

Dosage and Administration

Adults

Dosage range is 1.5g - 6g daily in three divided doses.

Usual dose

500mg to 1g by intravenous administration 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 1g every 8 hours.
2. Meningitis - the dose should be 2g 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 infections.

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

Meropenem Sandoz should be given as an intravenous bolus injection over approximately 5 minutes or by intravenous infusion over approximately 15 to 30 minutes (see Method of administration). There is limited safety data available to support the administration of a 2g bolus dose.

Dosage schedule for adults with impaired renal function

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

Creatinine Clearance (mL/min)	Dose (based on unit doses of 500mg, 1g, 2g 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 and haemofiltration. If continued treatment with Meropenem Sandoz 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.

Use in adults with hepatic insufficiency

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

Use in the elderly

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

Paediatric use

For infants and children over 3 months and up to 12 years of age 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. In children over 50kg weight, adult dosage should be used.

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.

Meropenem Sandoz should be given as an intravenous bolus over approximately 5 minutes or by intravenous infusion over approximately 15 to 30 minutes. There is limited safety data available to support the administration of a 40 mg/kg bolus dose.

There is no experience in children with renal impairment.

Method of administration

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

Meropenem Sandoz for intravenous infusion may be directly constituted with a compatible infusion fluid (see Compatibility and stability) and then further diluted (50 to 200 mL) with the compatible infusion fluid, as needed.

Shake constituted solution before use. All vials are for use in one patient on one occasion only. Standard aseptic technique should be employed during constitution and administration.

Compatibility and stability

Meropenem Sandoz is compatible with the following infusion fluids:

- 0.9% sodium chloride
- 10% glucose
- 5% glucose with 0.02% sodium bicarbonate
- 0.9% sodium chloride and 5% glucose
- 5% glucose with 0.15% potassium chloride
- 10% mannitol
- Normosol-M in 5% glucose.

Contraindications

Meropenem Sandoz powder for injection is contraindicated in patients who have demonstrated hypersensitivity to meropenem or other carbapenems, penicillins or other β -lactam antibiotics or any component of this product.

Warnings and Precautions

Hypersensitivity effects (allergic/anaphylaxis)

Serious and occasionally fatal hypersensitivity reactions have been reported in patients receiving therapy with β -lactams. 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 occurs to meropenem then discontinue the medicine. Serious hypersensitivity reactions may require adrenaline and other emergency measures.

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

Pseudomembranous colitis has been observed with practically all antibiotics and may vary in severity from slight to life-threatening. Therefore, antibiotics should be prescribed with care for individuals with a history of gastrointestinal complaints, particularly colitis. 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 medicine 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. Medicines which delay peristalsis, e.g. opiates and diphenoxylate with atropine (Lomotil) may prolong and/or worsen the condition and should not be used.

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. A positive or indirect Coombs' test may develop.

The concomitant use of valproic acid/sodium valproate and meropenem is not recommended (see Interactions with other medicines). Meropenem may reduce serum valproic acid levels. Subtherapeutic levels may be reached in some patients.

Effects on fertility

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

Use in pregnancy (Category B2)

Reproduction studies conducted with meropenem in rats have shown no embryotoxicity or teratogenicity at plasma exposures (based on AUC values) approximately equal to those observed in patients at the recommended intravenous dose. In a teratology study in cynomolgus monkeys given daily intravenous injections meropenem showed no evidence of teratogenicity at dose levels up to 360mg/kg/day.

There are however, no adequate or well controlled trials of meropenem in pregnant women. Because reproduction studies are not always predictive of human response, Meropenem should not be used in pregnancy unless the potential benefit justifies the potential risk to the foetus.

Use in lactation

Meropenem is detectable at very low concentrations in animal breast milk. Meropenem should not be used in breast-feeding women unless the potential benefit justifies the potential risk to the baby.

Paediatric use

Efficacy and tolerability in infants under 3 months of age have not been established; therefore,

meropenem is not recommended for use below this age.

Use in patients with renal insufficiency

See Dosage and administration.

Use in patients with liver disease

Patients with pre-existing liver disorders should have liver function monitored during treatment with Meropenem.

Carcinogenicity

The carcinogenic potential of meropenem has not been investigated.

Genotoxicity

Meropenem, with and without metabolic activation as appropriate, was not genotoxic in assays for gene mutations (*Salmonella typhimurium*, *E. coli* and Chinese hamster ovary cells) and chromosomal damage (mouse micronucleus assay and human lymphocytes *in vitro*).

Effects on ability to drive and use machinery

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.

Adverse Effects

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.

The following adverse effects have been identified following clinical studies with Meropenem. Their frequency is presented in Table 1 - Frequency of Adverse Effects (data derived from clinical trial data sources) using CIOMS III frequency classification and then listed by MedDRA SOC and at the preferred level. Frequencies of occurrence of undesirable effects are defined as: very common ($\geq 1/10$; $\geq 10\%$); common ($\geq 1/100$ to $< 1/10$; $\geq 1\%$ to $< 10\%$); uncommon ($\geq 1/1,000$ to $< 1/100$; $\geq 0.1\%$ to $< 1\%$); rare ($\geq 1/10,000$ to $< 1/1,000$; $\geq 0.01\%$ to $< 0.1\%$); very rare ($< 1/10,000$; $< 0.01\%$).

Table 1 – Frequency of Adverse Effects (data derived from clinical trial data sources)¹.

System Organ Class	Frequency	Adverse Effect
Infections and infestations	uncommon	oral and vaginal candidiasis
Blood and lymphatic system disorders	common uncommon	thrombocythaemia eosinophilia, thrombocytopenia, leucopenia, neutropenia
Nervous system disorders	common uncommon rare	headache parasthesiae convulsions
Gastrointestinal disorders	common	diarrhoea, vomiting, nausea
Hepatobiliary disorders	common uncommon	alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased, blood lactate dehydrogenase increased, gamma- glutamyltransferase increased blood bilirubin increased
Skin and subcutaneous tissue disorders	common uncommon	rash, pruritis urticaria
General disorders and administration site conditions	common uncommon	inflammation, pain thrombophlebitis

¹ 1999 Norrby SR and Gildon KM. Safety Profile of Meropenem: a review of nearly 5000 patients treated with Meropenem; Sand J infect Dis 1999; 31: 3-10 and the integrated Summary of Safety 1993.

The following adverse effects have been identified from post-marketing clinical trials and spontaneous reports. Their frequency is presented in Table 2 – Reporting Rate of Adverse Effects (data derived from a combination of post-marketing clinical trial and spontaneous sources) using CIOMS III frequency classification and then listed by MedDRA SOC and at the preferred level. Frequencies of occurrence of undesirable effects are defined as: very common ($\geq 1/10$; $\geq 10\%$); common ($\geq 1/100$ to $< 1/10$; $\geq 1\%$ to $< 10\%$); uncommon ($\geq 1/1,000$ to $< 1/100$; $\geq 0.1\%$ to $< 1\%$); rare ($\geq 1/10,000$ to $< 1/1,000$; $\geq 0.01\%$ to $< 0.1\%$); very rare ($< 1/10,000$; $< 0.01\%$).

Table 2 - Reporting Rate of Adverse Effects (data derived from a combination of post-marketing clinical trial and spontaneous sources)

System Organ Class	Frequency	Adverse Effect
Blood and lymphatic system disorders	rare very rare	agranulocytosis haemolytic anaemia
Immune system disorders	very rare	angioedema, manifestations of anaphylaxis
Gastrointestinal disorders	very rare	pseudomonas colitis
Skin and subcutaneous tissue disorders	common	toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme

Interactions

Meropenem has been administered concomitantly with many other medications without apparent adverse interaction. However, no specific drug 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 medicines 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

Decreases in blood levels of valproic acid have been reported when it is co-administered with carbapenem agents resulting in a 60-100% decrease in valproic acid levels in about two days. Due to the rapid onset and the extent of the decrease, co-administration of meropenem in patients stabilised on valproic acid/sodium valproate is not considered to be manageable and therefore should be avoided (see Precautions).

Overdose

Contact the Poisons Information Centre on 0800 POISON or 0800 764766 for advice on management of 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. Limited post-marketing experience indicates that if adverse events occur following overdosage, they are consistent with the adverse event profile described in Adverse Effects and are generally mild in severity and resolve on withdrawal or dose reduction. 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.

Further Information

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 not 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.

Pharmaceutical Precautions

Special precautions for storage

Meropenem Sandoz should not be mixed with or physically added to solutions containing other medicines.

Prior to constitution, store Meropenem Sandoz powder for injection below 30°C.

To reduce microbiological hazard, solutions of meropenem should be used as soon as practicable after reconstitution. If storage is necessary, hold at 2°C to 8°C for not more than 24 hours, or the period shown in the following table, whichever is the lesser.

Diluent	Maximum recommended storage period from reconstitution (hours)	
	20 - 25°C	2 - 8°C
<i>Vials constituted with Water for Injection for bolus injection</i>	8	24
<i>Solutions (1 to 20mg/mL) prepared with:</i>		
0.9% sodium chloride	8	24
5% glucose and 0.9% sodium chloride	3	14
5% glucose and 0.15% potassium chloride	3	14
10% mannitol	3	14
Normosol-M in 5% glucose	3	14
10% glucose	2	8
5% glucose and 0.02% sodium bicarbonate	2	8

Solutions of Meropenem Sandoz should not be frozen.

Shelf life

2 years

Package Quantities

Meropenem 500mg Powder for Injection – 20mL clear glass vial with rubber stopper, containing a white to pale yellow powder. Available in packs of 10 vials.

Meropenem 1g Powder for Injection – 30mL clear glass vial with rubber stopper, containing a white to pale yellow powder. Available in packs of 10 vials.

Medicine Classification

Prescription Medicine

Name and Address

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Date of Preparation

02 November 2011