240 X 130 MM - WITHOUT FOLDING- 60GSM

VENMERO

Meropenem Powder for solution for injection or infusion USP 500mg/1000mg

DESCRIPTION
White to yellowish powder.
After reconstitution & dilution: Light Yellow Solution.
The product is compatible with sterile Water for Injections as the injection solution.
The product is compatible with 0.9% sodium chloride solution for infusion or 5% glucose (dextrose) solution for infusion as the infusion solution.

COMPOSITION
VENMERO Meropenem Powder for Solution for Injection or Infusion 500 mg:
Each vial contains sterile Meropenem Trihydrate
equivalent to 500 mg Anhydrous Meropenem.
VENMERO Meropenem 1g Powder for Solution for Injection or Infusion:
Each vial contains sterile Meropenem Trihydrate
equivalent to 1 g Anhydrous Meropenem.
For each gram of meropenem (anhydrous potency) the vial contains 90.2 mg (3.92 mmol) of sodium

PHARMACODYNAMIC PROPERTIES
Meropenem exerts its bactericidal activity by inhibiting bacterial cell wall synthesis in Gram-positive and Gram- negative bacteria through binding to penicillin-binding proteins (PBPs).
Pharmacokinetic/Pharmacodynamic (PK/PD) relationship:
Similar to other beta-lactam antibacterial agents, the time that meropenem concentrations exceed the MIC (T>MIC) has been shown to best correlate with efficacy.
The following table of pathogens listed is derived from clinical experience and therapeutic guidelines.
Commonly susceptible species:
Gram-positive aerobes:
Enterococcus faecalis[$], *Staphylococcus aureus (methicillin-susceptible)£, Staphylococcus species (methicillin- susceptible) including Staphylococcus epidermidis, Streptococcus agalactiae (Group B), Streptococcus milleri group (S. anginosus, S. constellatus, and S. intermedius), Streptococcus pneumoniae, Streptococcus pyogenes* (Group A)
Gram-negative aerobes:
Citrobacter freundii, Citrobacter koseri, Enterobacter aerogenes, Enterobacter cloacae Escherichia coli, Haemophilus influenzae, Klebsiella oxytoca, Klebsiella pneumoniae Morganella morganii, Neisseria meningitides, Proteus mirabilis, Proteus vulgaris, Serratia marcescens.
Gram-positive anaerobes:
Clostridium perfringens, Peptoniphilus asaccharolyticus, Peptostreptococcus species (including P. micros, P anaerobius, P. magnus)
Gram-negative anaerobes:
Bacteroides caccae, Bacteroides fragilis group, Prevotella bivia, Prevotella disiens
Species for which acquired resistance may be a problem Gram-positive aerobes:
Enterococcus faecium[$]
Gram-negative aerobes:
Acinetobacter species, Burkholderia cepacia, Pseudomonas aeruginosa
Inherently resistant organisms Gram-negative aerobes:
Stenotrophomonas maltophilia, Legionella species
Other micro-organisms
Chlamydophila pneumoniae, Chlamydophila psittaci, Coxiella burnetii, Mycoplasma pneumoniae
[$]Species that show natural intermediate susceptibility
[£]All methicillin-resistant staphylococci are resistant to meropenem

PHARMACOKINETIC PROPERTIES
A 30 minute intravenous infusion of a single dose of meropenem results in peak plasma levels of approximately 11 µg/mL for the 250 mg dose, 23 µg/mL for the 500 mg dose and 49 µg/mL for the 1g dose.
There is no absolute pharmacokinetic proportionality with the administered dose both as regards Cmax and AUC. A reduction in plasma clearance from 239 to 205 mL/min for the range of dosage 500 mg to 2 g has been observed.
A 5 minute intravenous bolus injection of meropenem results in peak plasma levels of approximately 52 µg/mL for the 500 mg dose and 112 µg/mL for the 1g dose. After an intravenous dose of 500 mg, plasma levels of meropenem decline to values of 1 µg/mL or less, 6 hours after administration.
In patients with normal renal function, meropenem's elimination half-life is approximately 1 hour.
Plasma protein binding of meropenem is approximately 2%.
Approximately 70% of the administered dose is recovered as unchanged meropenem in the urine over 12 hours, after which little further urinary excretion is detectable. Urinary concentrations of meropenem in excess of 10 µg/mL are maintained for up to 5 hours after the administration of a 500 mg dose. No accumulation of meropenem in plasma or urine was observed with regimens using 500 mg administered every 8 hours or 1 g administered every 6 hours in patients with normal renal function.
The only metabolite of meropenem is microbiologically inactive.
Meropenem penetrates well into most body fluids and tissues including cerebrospinal fluid of patients with bacterial meningitis, achieving concentrations in excess of those required to inhibit most bacteria.
Paediatric population
The pharmacokinetics in infants and children with infection at doses of 10, 20 and 40 mg/kg showed Cmax values approximating to those in adults following 500, 1000 and 2000 mg doses, respectively. The doses and half-lives of paediatric population are similar to those in adults in all but the youngest (<6 months t1/2 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 interindividual 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.
Renal Insufficiency The plasma clearance of meropenem correlates with creatinine clearance. Dosage adjustments are necessary in subjects with renal impairment
Elderly
A reduction in plasma clearance of meropenem have shown in the elderly which correlated with age-associated reduction in creatinine clearance.
Liver Disease
No effects of liver disease are shown on the pharmacokinetics of meropenem in patients with liver disease.

INDICATIONS
Meropenem IV is indicated for treatment, in adults and children, of the following infections caused by single or multiple bacteria sensitive to meropenem.
• Pneumonias and Nosocomial pneumonias
• Urinary Tract Infections
• Intra-abdominal Infections
• Gynaecological Infections, such as endometritis and pelvic inflammatory disease.
• Bacterial Meningitis
• Septicaemia
• Empiric treatment, for presumed infections in patients with febrile neutropenia, used as monotherapy or in combination with anti-viral or anti-fungal agents.
Meropenem IV is efficacious alone or in combination with other antimicrobial agents in the treatment of polymicrobial infections.

CONTRAINDICATIONS
Meropenem Powder for Solution for Injection or Infusion is contraindicated in patients who have demonstrated hypersensitivity to this product.

WARNINGS AND PRECAUTIONS
Partial cross-allergenicity between other carbapenems and beta-lactam antibiotics, penicillins and cephalosporins may occur. Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions (SCAR)) may develop in patients receiving therapy with beta lactams. Before initiating therapy with meropenem, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, carbapanems or other beta-lactam agents. If an allergic reaction occurs, meropenem must be discontinued immediately and appropriate alternative therapy instituted.
SCAR, such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), erythema multiforme (EM) and acute generalized exanthematous pustulosis (AGEP) occur in patients receiving meropenem. If signs and symptoms suggestive of these reactions appear, meropenem should be withdrawn immediately and an alternative treatment should be considered.
Use of meropenem in patients with hepatic disease should be made with careful monitoring of transaminase and bilirubin levels.
As with other antibiotics, overgrowth of non-susceptible organisms may occur and, therefore, continuous monitoring of each patient is necessary.
Use in infections caused by methicillin resistant staphylococci is not recommended.
Rarely, pseudomembranous colitis due to meropenem as 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 gastro- intestinal complaints, particularly colitis.
It is important to consider the diagnosis of pseudomembranous colitis in the case of patients who develop diarrhoea in association with the use of meropenem. Although toxin produced by Clostridium difficile is one of the main causes of antibiotic-associated colitis, other causes should be considered.
The co-administration of meropenem with potentially nephrotoxic drugs should be considered with caution.
The concomitant use of valproic acid/sodium valproate and meropenem is not recommended. Meropenem may reduce serum valproic acid levels. Subtherapeutic levels may be reached in some patients.
Paediatric use
Efficacy and tolerability in infants under 3 months old have not been established; therefore, meropenem is not recommended for use below this age. There is no experience in children with altered hepatic or renal function.
Keep all medicines away from children.
Meropenem contains sodium.
Meropenem 500: This medicinal product contains 45 mg sodium per 500 mg, equivalent to 2.25% of the WHO recommended maximum daily intake of 2 g sodium for an adult.
Meropenem 1000: This medicinal product contains 90 mg sodium per 1000 mg, equivalent to 4.5% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

PREGNANCY AND LACTATION
Pregnancy
Limited amount of data on the safety of meropenem in human pregnancy. Meropenem should not be used in pregnancy unless the potential benefit justifies the potential risk to the foetus. In every case, it should be used under the direct supervision of the physician.
Lactation
Meropenem has been reported to be excreted in human milk. Meropenem should not be used in breast-feeding women unless the potential benefit justifies the potential risk to the baby.

DRUG INTERACTIONS
Probenecid competes with meropenem for active tubular secretion and thus inhibits the renal excretion, 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. The protein binding of meropenem is low (approximately 2%) and, therefore, no interactions with other compounds based on displacement from plasma proteins would be expected.
Meropenem may reduce serum valproic acid levels. Subtherapeutic levels may be reached in some patients.
Co-administration of valproic acid with carbapenem agents resulting in a 60-100% decrease in valproic acid levels in blood for about two days. Due to the rapid onset and the extent of the decrease, co-administration of meropenem in patients stabilized on valproic acid is not considered to be manageable and therefore should be avoided

MAIN SIDE/ADVERSE EFFECTS

System Organ Class	Frequency	Event
Infections and infestations	Uncommon	oral and vaginal candidiasis
Blood and lymphatic system disorders	Common	thrombocythaemia
	Uncommon	eosinophilia, thrombocytopenia, leucopenia, neutropenia
	Rare	agranulocytosis
	Very Rare	haemolytic anaemia
Immune system disorders	Very Rare	angioedema, manifestations of anaphylaxis
Psychiatric disorders	Rare	delirium
Nervous system disorders	Common	headache
	Uncommon	paraesthesiae
	Rare	convulsions
Gastrointestinal disorders	Common	diarrhoea, vomiting, nausea
	Very Rare	pseudomembraneous colitis
Hepatobiliary disorders	Common	alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased, blood lactate dehydrogenase increased, gamma-glutamyltransferase increased
	Uncommon	blood bilirubin increased
Skin and subcutaneous tissue disorders	Common	rash, pruritis
	Uncommon	urticaria,
	Very Rare	toxic epidermal necrolysis, Stevens Johnson syndrome, erythema multiforme
	Not Known	Drug Reactions with Eosinophilia and Systemic Symptoms (DRESS Syndrome), acute generalized exanthematous pustulosis (AGEP)
General disorders and Administration site conditions	Common	inflammation, pain
	Uncommon	thrombophlebitis

OVERDOSE AND TREATMENT
Relative overdose may be possible in patients with renal impairment if the dose is not adjusted. Limited post-marketing experience indicates that if adverse reactions occur following overdose, they are consistent with the adverse reaction profile described below, are generally mild in severity and resolve on withdrawal or dose reduction. Symptomatic treatments should be considered. In individuals with normal renal function, rapid renal elimination will occur.
Haemodialysis will remove meropenem and its metabolite.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINE
No studies on the effect 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, paresthesia and convulsions have been reported for meropenem.

DOSAGE AND ADMINISTRATION
Adults
The dosage and duration of therapy shall be established depending on type and severity of infection and the condition of the patient.
The recommended daily dosage is as follows:
500 mg IV every 8 hours in the treatment of pneumonia, UTI, gynaecological infections such as endometritis.
1 g IV every 8 hours in the treatment of hospital acquired pneumonias, peritonitis, presumed infections in febrile neutropenic patients, septicaemia.
In meningitis the recommended dosage is 2 g every 8 hours.
A dose of up to 2 g three times daily in adults and adolescents and a dose of up to 40 mg/kg three times daily in children may be particularly appropriate when treating some types of infections, such as nosocomial infections due to Pseudomonas aeruginosa.
Regular sensitivity testing is recommended when treating Pseudomonas aeruginosa infection.
There are limited safety data available to support the administration of a 2 g dose in adults as an intravenous bolus injection.
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. There are limited data to support the application of these dose adjustments for a unit dose of 2 g.

Creatinine Clearance (ml/min)	Dose (based on unit doses of 500 mg, 1 g, 2 g)	Frequency
26 - 50	one unit dose	every 12 hours
10 - 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 is necessary, it is recommended that the unit dose (based on the type and severity of infection) is administered at the completion of the haemodialysis procedure to restore therapeutically effective plasma concentrations.
There is no experience with the use of Meropenem in patients under peritoneal dialysis.
Dosage in Adults with Hepatic Insufficiency
No dosage adjustment is necessary in patients with hepatic insufficiency
Elderly Patients
No dosage adjustment is required for the elderly with normal renal function or creatinine clearance values above 50 mL/min.
Children
For children over 3 months and up to 12 years of age the recommended dose is 10 - 20 mg/kg every 8 hours depending on type and severity of infection, susceptibility of the pathogen and the condition of the patient. In children over 50 kg weight, adult dosage should be used.
In meningitis the recommended dose is 40 mg/kg every 8 hours.
Febrile episodes in neutropenic patients-the dose should be 20 mg/kg every 8 hours. There is no experience in children with renal impairment.
There are limited safety data available to support the administration of a 40 mg/kg dose in children as an intravenous bolus injection.
Method of administration
VENMERO can be given as an intravenous bolus injection over approximately 5 minutes or by intravenous infusion over approximately 15 to 30 minutes using the specific available presentations.
VENMERO to be used for bolus intravenous injection should be constituted with sterile Water for Injections (5 mL per 250 mg Meropenem). This provides an approximate concentration of 50 mg/mL. Constituted solutions are light yellow solution.
Bolus injection: A solution for bolus injection is prepared by dissolving the drug product VENMERO in water for injection to a final concentration of 50 mg/ml. Chemical and physical in-use stability for a prepared solution for bolus injection has been demonstrated for 3 hours at up to 25°C or 12 hours under refrigerated conditions (2-8°C).
From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbiological contamination, the product should be used immediately.
If not used immediately in-use storage times and conditions are the responsibility of the user.
Infusion: A solution for infusion is prepared by dissolving the drug product VENMERO in either 0.9% sodium chloride solution for infusion or 5% glucose (dextrose) solution for infusion to a final concentration of 1 to 20 mg/ml.
Chemical and physical in-use stability for a prepared solution for infusion using 0.9% sodium chloride solution has been demonstrated for 3 hours at up to 25°C or 24 hours under refrigerated conditions (2-8°C).
From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbiological contamination, the product should be used immediately.
If not used immediately, in-use storage times and conditions are the responsibility of the user.
Constituted solution of VENMERO in 5% glucose (dextrose) solution should be used immediately.
The constituted solutions should not be frozen.
If not used immediately, in-use storage times and conditions are the responsibility of the user.

Special Precaution while Handling and Disposal
Each vial is for single use only. Standard aseptic techniques should be used for solution preparation and administration. The solution should be shaken before use. Any unused product or waste material should be disposed of in accordance with local requirements.

INCOMPATIBILITIES
This medicinal product must not be mixed with other medicinal products except those used to dilute meropenem powder for injection.
Storage: Store below 30°C. Protect from light & moisture. Do not freeze the reconstituted solution.
After reconstitution:
Water for Injection
Chemical and physical in-use stability for a prepared solution for bolus injection using water for injection has been demonstrated for 3 hours at up to 25°C or 12 hours under refrigerated conditions (2-8°C).
0.9% sodium chloride solution
Chemical and physical in-use stability for a prepared solution for infusion using 0.9% sodium chloride solution has been demonstrated for 3 hours at up to 25°C or 24 hours under refrigerated conditions (2-8°C).
5% dextrose solution
Reconstituted solution of the product in 5% dextrose solution should be used immediately.
The constituted solutions should not be frozen.

Presentation / Packing:
VENMERO is supplied in 10 ml and 20 ml tubular clear Type 1 glass vial containing sufficient meropenem to deliver 500 mg or 1000 mg for intravenous administration, respectively.

Manufactured by
VENUS REMEDIES LIMITED
Hill Top Industrial Estate, Jharmajri, EPIP Phase-I (Extn.), Bhatoli Kalan, Baddi,
Distt. Solan, Himachal Pradesh, 173205, India

Product Registration Holder
Unimed SDN. Bhd.
No. 53, Jalan Tembaga SD 5/2B, Bandar Sri Damansara, 52200, Kuala Lumpur, Malaysia.

Date of First Authorisation/Renewal of the Authorisation
NA
Date of Revision
13 April 2026