Dosage in Renal impairment
In patients with impaired renal function (creatinine clearance < 51 ml/min), the dose of should be adjusted to compensate for the slower rate of renal elimination.
Dosage in Hepatic Impairment
Patients with hepatic impairment do not require adjustment of Meropenem dosage.

Reconstitution of Single dose Vials for Intravenous bolus / Infusion Administration

vial content	Amount of Diluent to be added (ml).
500 mg	10
1 gm	20

The vial should be shaken until dissolution occurs and then allowed to stand until the solution is clear.
For Intravenous bolus administration the resultant solution may then be injected over a 3 - 5 minute period.
For Intravenous infusion, constitute the 500 mg or 1 gm vial and dilute it with one of the compatible IV fluids to provide solutions containing approximately 2.5 - 50 mg/ml (10 - 200 ml for 500 mg and 20 - 400 for 1 gm) of the drug and should be infused IV over 15 - 30 minutes.

COMPATIBILITY AND STABILITY
Compatible fluids include 5% or 10% dextrose, 0.9% sodium chloride, 5% dextrose and 0.9% or 0.225% sodium chloride, 5% dextrose and 0.15% potassium chloride, 5% dextrose and 0.02% sodium bicarbonate, 2.5% or 10% mannitol. Solutions should be freshly prepared and used.
Meropenem constituted as directed is stable for 1 - 4 hours at controlled room temperature 15° - 25°C (59° - 77°F) or for 2- 24 hours at 4°C (39°F) depending on IV fluids used. Stability is maximum for 0.9% sodium chloride and Ringer's lactate solution.

CONTRAINDICATIONS
Meropenem is contraindicated in patients who have shown immediate hypersensitivity reactions to penicillins or other β-lactam antibiotics.

WARNINGS
1. Hypersensitivity reactions
2. Pseudomembraneous colitis.

PRECAUTIONS
Seizure Potential
A tolerability concern with carbapenems is their potential to cause CNS toxicity and seizures. Meropenem appears to be associated with a risk of seizures, particularly in those with underlying CNS pathology. This risk is less than Imipenem.

Usage in Pregnancy Pregnancy Category B
There are no adequate and well-controlled studies of meropenem use in pregnant women and should be used during pregnancy only if clearly needed.

Nursing mothers
It is not known whether meropenem is excreted in human breast milk. Caution should be exercised when MIROXAM is administered to a nursing women.

Pediatric Use
The safety and efficacy of in the treatment of meningitis has been established in patients only > 3 months of age.

In Elderly
No special problems yet evident. Renal excretion of meropenem and its ring-open metabolite are slowed in the elderly, in keeping with the decline of renal function, and the dosage interval should be reduced accordingly.

ADVERSE EFFECTS
Potentially Life-threatening Effects
No life-threatening effects have yet been reported but rare anaphylactic reactions may be anticipated. Serious hypersensitivity reactions are the most likely, but the incidence, if any, is not yet known.
Symptomatic Adverse Effects
Rashes (2.3%), headache (2%), nausea (3.5%) and diarrhea (4.3%) have been observed in short term clinical trials. There may be pain, phlebitis and oedema at the injection site. As with other broad spectrum antimicrobial agents, candidiasis may occur.

OVERDOSE
This has not been reported and is less likely to occur with parenterally administered drug. In view of the results of acute toxicity tests, this is unlikely to be a problem. Appropriate supportive therapy is recommended.

DRUG INTERACTIONS
Probencid competes with the renal tubular secretion of meropenem and increases the half-life by about one third.
Administration of meropenem to patients taking sodium valproate may result in the reduction of serum valproic acid levels. Subtherapeutic levels of valproic acid may be reached in some patients.

Storage:
Store protected from moisture at a temperature not exceeding 30°C.

PRESENTATION
A vial of 500 mg with 10 ml ampoule of Sterile Water for Injections IP in a box.
A vial of 1 gm with 20 ml ampoule of Sterile Water for Injections IP in a box.

Manufactured by :
PROTECH TELELINKS
(A WHO-GMP Certified Co.)
Mauza Ogli, Sukeli Road,
Kala Amb, District Siramour,
Himachal Pradesh - 173030
INDIA

Marketed by :
BIOMAK
Laboratories Pvt. Ltd
Plot No. 3B(A), Industrial Area,
Phase 3, Sansarpur Terrace
Growth Centre, Dist. Kangra,
Himachal Pradesh - 176501,
INDIA

Visit the address or
mail to info@biomaklaboratories.com

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

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Meropenem Injection IP 500/1000 mg

Probinem

INJECTION

Composition:
Each Vial Contains:
Meropenem Sterile IP
Eq. to anhydrous Meropenem 500 mg
Sodium Carbonate IP
Eq. to Sodium 45.1 mg
(A Sterile mixture of Meropenem IP
(& Sodium Carbonate IP)

Composition:
Each vial contains:
Meropenem (Sterile) IP
Eq. to anhydrous Meropenem 1000 mg
Sodium Carbonate IP
Eq. to Sodium 90.20 mg
(A Sterile mixture of Meropenem IP
& Sodium Carbonate IP)

DESCRIPTION
Meropenem is a synthetic carbapenem antibiotic. Unlike Imipenem, Meropenem has a methyl group at position 1 of the 5-membered ring, which confers stability against hydrolysis by dehydrolysis by dehydropeptidase 1 (DHP-1) present on the brush border of proximal renal tubular cells and therefore does not require concomitant administration with a DHP-1 inhibitor such as Cilastatin. Chemically meropenem is (4R,5S,6S)-3-[(3S,5S)-5-(Dimethylcarbamoyl)-3-pyrrolidinyl]thio]-6-[(1R)-1-hydroxyethyl]-4-methyl-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic
acid trihydrate. Its chemical formula is $C_{17}H_{25}N_3O_5S.3H_2O$ and molecular weight is 437.5.

PHARMACOLOGY
Meropenem is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis. Antibacterial action of Meropenem is related to binding of the drug to penicillin binding proteins (PBPs) of Gram-positive and Gram-negative organisms. The high resistance of meropenem to most bacterial β-lactamases and good penetration of the drug through the outer membrane also contribute significantly to antimicrobial activity. Meropenem may be less of an inducer of β-lactamases than Imipenem.

MICROBIOLOGY
Meropenem shares the very broad antibacterial spectrum of Imipenem. Clinically useful activity extends to the following types of bacteria : virtually all genera of the family Enterobacteriaceae; most anaerobic and anaerobic Gram-positive cocci (Haemophilus spp., Neisseria spp., etc); most isolates of Bacteroides fragilis and other anarobic Gram-negative bacilli. In vitro Meropenem exerts a greater activity than Imipenem against Enterobacteriaceae (2 to 32 fold) and most pseudomonas (2 to 4 fold) whereas it is slighthy less active against Gram-positive species. Its activity against anaerobic Gram-negative rods is very similar to that of meropenem.Meropenem does not exhibit any useful activity against mycoplasmas, obligate intracellular bacteria such as chlamydiae and rickettsiae, and mycobacteriae. Activity against Mycobacterium avium complex is known to be poor.

PHARMACOKINETICS
Meropenem is not absorbed when given orally and is normally administered by intravenous route. Peak plasma concentrations immediately after the completion of the infusion are 50 - 60 mg/lt after a 1 g dose and 20 - 25 mg/lt after 500 mg. One hour after a 5 min. infusion of 1 gm to healthy subjects average plasma concentrations are about 24 mg/lt and decline to 0.7 mg/lt at 6 h.
The plasma half life is approximately 1h, estimates for the mean varying from 0.9 to 1.2 h.
Meropenem is rapidly distributed throughout the body. The volume of distribution in humans is relatively low, only 0.3-0.4 lt/kg. Approximately 25% of an intravenous dose of Meropenem is converted to the antibacterially inactive ring-open form by hydrolysis of the β-lactam ring, catalysed by renal dehydropeptidase 1 (DHP-1). Meropenem is four times more resistant to human DHP-1 than Imipenem.
The metabolite is excreted essentially only via the kidneys. Upto 80% of a dose is excreted urine; the majority of the dose is excreted in the first 4h.
The pharmacokinetics of meropenem in children 1 year and older are very similar to those in adults with a half-life of approximately 0.8-1.1h. Upto 70% of the dose is eliminated in the urine during the first 6h after dosing. The half-life was 2.95h in preterm neonates and 2.04h in full term neonates.
The half life of Meropenem in elderly subjects with normal renal functions for their age is approximately 50% longer than in young healthy adults.

THERAPEUTIC INDICATIONS
is indicated in the treatment of :
1. Nosocomial Pneumonia
2. Urinary Tract infections
3. Intra Abdominal infections
4. Gyanecological infections
5. Skin and Skin Structure infections
6. Meningitis
7. Septicaemia
8. Empiric treatment of Adult Febrile Neutropenia
Culture and susceptibility testing should be performed where appropriate to determine the susceptibility of the causative microoraganism(s) to Meropenem.
Therapy with may be instituted before results of susceptibility studies are known; however, once these results become available, the antibiotic treatment should be adjusted accordingly.

DOSAGE & ADMINISTRATION
is administered intravenously as a bolus injection given over 3 - 5 mins, or by infusion over 15 - 30 mins.
For adults with normal renal function the usual dose is 0.5 - 1 gm every 8 hourly.
For the treatment of adult meningitis, the dose is increased to 2 gm every 8 hourly.
A dose of 10 - 20 mg/kg every 8 hourly is recommended for children under 12 years.
In meningitis, the pediatric dose of 40 mg/kg every 8 hourly is recommended.
In chlidren over 50 kg body weight the adult dosage should be given.