Carbanem™

Meropenem USP

50012

Presentation:
Carbanem 1g: Each vial contains sterile mixture of meropenem and sodium carbonate equivalent to 1.0g of Anhydrous Meropenem USP.

Carbanem 500mg: Each vial contains sterile mixture of meropenem and sodium carbonate equivalent to 500mg of Anhydrous Meropenem USP.

Description and Mode of action:
Meropenem exerts its action by penetrating bacterial cells readily and interfering with the synthesis of vital cell wall components, which leads to cell death.

Pharmacokinetics:
At the end of a 30-minute intravenous infusion of a single dose of Meropenem IV in normal volunteers, mean peak plasma concentrations are approaximately 23µg/ml (range 14-26) for 500mg dose and 49µg/ml (range 39-58) for 1g dose. A 5-minute intravenous bolus injection of Meropenem IV in normal volunteers results in mean peak plasma concentrations of approximately 45µg/ml (range 18-65) for the 500mg dose and 112 µg/ml (range 83-140) for the 1g dose.

Following intravenous doses of 500 mg mean plasma concentrations of Meropenem usually decline to approximately 1 µg/ml at 6 hours after administration. In subjects with normal renal function, the elimination half-life of Meropenem IV is approximately 1 hour. Approximately 70% of the intravenously administered dose is recovered as uncharged 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 a 500 mg dose. No accumulation of Meropenem in plasma or urine was observed with regimens using 500 mg administered every 8 hours or 1g administered every 6 hours in volunteers with normal renal function.

Plasma protein binding of Meropenem is approximately 2%. There is one metabolite which is microbiologically inactive.

Meropenem penetrates well into most body fluids and tissues including cerebrospinal fluid, achieving concentrations matching or exceeding those required to inhibit most susceptible bacteria. After a single intravenous dose of Meropenem IV, the highest mean concentrations of Meropenem were found in tissues and fluids at 1 hour (0.5 to 1.5 hours) after the start of infusion, except where indicated in the tissues and fluids listed in the table below.

Table 1. Meropenem Concentrations in Selected Tissues (Highest Concentrations Reported)

Tissue	IV Dose (g)	Number of samples	Mean [µg/ml or µg/g] *	Range [µg/ml or µg/g]
Endometrium	0.5	7	4.2	1.7-10.2
Myometrium	0.5	15	3.8	0.4-8.1
Ovary	0.5	8	2.8	0.8-4.8
Cervix	0.5	2	7.0	5.4-8.5
Fallopian tube	0.5	9	1.7	0.3-3.4
Skin	0.5	22	3.3	0.5-12.6
Interstitial fluid**	0.5	9	5.5	3.2-8.6
Skin	1.0	10	5.3	1.3-16.7
Interstitial fluid**	1.0	5	26.3	20.9-37.4
Colon	1.0	2	2.6	2.5-2.7
Bile	1.0	7	14.6 (3h)	4.0-25.7
Gall bladder	1.0	1		3.9
Peritoneal fluid	1.0	9	30.2	7.4-54.6
Lung	1.0	2	4.8 (2h)	1.4-8.2
Bronchial mucosa	1.0	7	4.5	1.3-11.1
Muscle	1.0	2	6.1 (2h)	5.3-6.9
Fascia	1.0	9	8.8	1.5-20
Heart valves	1.0	7	9.7	6.4-12.1
Myocardium	1.0	10	15.5	5.2-25.5
CSF (inflamed)	20 mg/kg ***	8	1.1 (2h)	0.2-2.8
	40 mg/kg ****	5	3.3 (3h)	0.9-6.5
CSF (uninflamed)	1.0	4	0.2 (2h)	0.1-0.3

* at 1 hour unless otherwise noted
** obtained from blister fluid
*** in paediatric patients of age 5 months to 8 years
**** in paediatric patients of age 1 month to 15 years

The Pharmacokinetics of Meropenem IV in paediatric patients of 2 years of age or older are essentially similar to those in adults. The elimination half-life for Meropenem was approximately 1.5 hours in paediatric patients of age 3 months to 2 years. The pharmacokinetics are linear over the dose range from 10 to 40 mg/kg.
Pharmacokinetic studies with Meropenem IV in patients with renal insufficiency have shown that the plama clearance of Meropenem correlates with creatinine clearance. Dosage adjustments are necessary in subjects with renal impairment. A pharmacokinetic study with Meropenem IV in elderly patients with Meropenem IV is hemodialyzable. However, there is no information on the usefulness of hemodialysis to treat overdose.
A Pharmacokinetic study with Meropenem IV in patients with hepatic impairment has shown no effects of liver disease on the pharmacokinetics of Meropenem.

Indications:
Pneumonias including nosocomial pneumonia, Urinary tract infections, Intra-abdominal infections, Gynaecological infections such as endomeritis and pelvic inflammatory disease, Skin and soft tissue infections, Meningitis, Septicemia.
Besides, empirical treatment for presumed infections in adult patients with febrile neutropenia used as immunotherapy or in combination with anti-viral or anti-fungal agents.
There is no experience in paediatric patients with neutropenia or primary or secondary immunodeficiency.

Contra-Indication:
History of hypersensitivity to the product

Side-Effects:
Along with its needed effects, a medicine may cause unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention.
Check with your doctor immediately if any of the following side effects occur :

More Common:
Redness and swelling at the site of injection

Less common:
Bluish lips or skin; chills; cold, clammy skin; confusion; dizziness; fainting; fast heartbeat; weak pulse; itching skin; light-headedness; not breathing; pain at place of injection; rapid, shallow breathing; skin rash and itching; sweating; wheezing

Rare:
Abdominal or stomach cramps and pain (severe); black, bloody, or tarry stools; black, bloody vomit; convulsions (seizures); diarrhoea (watery and severe), which may also be bloody; fever with or without chills; nosebleed; vomiting of blood or material that looks like coffee grounds

Precaution:
Caution in patients with history of hypersensitivity to carbapenems or other beta-lactam antibiotics. If an allergic reaction to Meropenem occurs, the drug should be discontinued and appropriate measures to be taken. Monitor transaminase and bilirubin levels when used in hepatic disease. Monitor for over growth of non-susceptible organisms as with other antibiotics. Caution in individuals with a history of gastrointestinal complaints, particularly colitis. In patients who develop diarrhoea, consider diagnosis of pseudo membraneous colitis. Caution if to be co-administered with potentially nephrotoxic drugs. Meropenem therapy may reduce serum valproic acid levels, sub-therapeutic levels may occur, 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 *P. aeruginosa* infection.

Dosage & Administration:

Adults:

The dosage and duration of therapy should be established depending on the type and severity of infection and the condition of the patient. The recommended daily dosage is as follows: Pneumonia, urinary tract infections, gynaecological infections such as endometritis, skin and skin structure infections: 500mg i.v. evey 8 hours. Nosocomial pneumonia, peritonitis, presumed infections in neutropenic and septicaemia: 1gm i.v. every 8 hours. Meningitis: 2g i.v. every 8 hours.

Hepatic impairment-no dosage adjustment is necessary in patients with hepatic insufficiency. Elderly patients-no dosage adjustment is required for elderly with normal renal function or creatinine clearance values above 50ml/min.

Renal impairment-dosage should be reduced in patients with creatinine clearance less than 51ml/min, as scheduled below:

Creatinine clearance (ml/min)	Dose (dependent on type of infection)	Frequency
26-50	Recommended dose	Every 12 hours
10-25	One-half recommended dose	Every 12 hours
<10	One-half recommended dose	Every 24 hours

Children:

For paediatric patients from 3 months of age and older, i.v. dose of meropenem is 10, 20 or 40 mg/kg every 8 hours (maximum dose is 2g every 8 hours), depending on the type of infection (complicated skin and skin structure, intra-abdominal or meningitis). (See dosing table below). Paediatric patients weighing over 50kg should be administered meropenem i.v. at a dose of 500mg every 8 hours for complicated skin and skin structure infections, 1g every 8 hours for intra-abdominal infections and 2g every 8 hours for meningitis. Meropenem i.v. should be given as intravenous infusion over approximately for 15 to 30 minutes or as an intravenous bolus injection (5 to 20ml) over approximately for 3-5 minutes.

Recommended i.v. dosage schedule of meropenem for paediatrics with normal renal function

Type of infection	Dosage (mg/kg)	Up to a Maximum Dose	Dosing Interval
Complicated skin and skin structure	10	500mg	Every 8 hours
Intra-abdominal	20	1g	Every 8 hours
Meningitis	40	2g	Every 8 hours

There is no experience in paediatric patients with renal impairment.

Administration:

Following reconstitution (5ml per 250mg) Meropenem should be given as an intravenous bolus injection over approx. For 5 minutes or by intravenous infusion (dilution in 50-200ml) over approx. For 15 to 30 minutes.

Drug Interaction:

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 probencid are adequate, the co-administration of probenecid with meropenem is not recommended. However, no specific drug interaction data are available.

Storage Condition: Store at a temperature not exceeding 25°C and in dry place protected from light. Reconstituted solution can be stored up to 2 hours at 15° to 25°C and up to 12 hours at 4°C.

Package Quantities:

Carbanem 1g: 1 vial of sterile mixture of meropenem and sodium carbonate equivalent to 1g Anhydrous Meropenem USP and 1 ampoule of 20ml Water for Injection BP for reconstitution with a sterile disposable syringe (20ml) and a butterfly needle.

Carbanem 500mg: 1 vial of sterile mixture of meropenem and sodium carbonate equivalent to 500mg Anhydrous Meropenem USP and 1 ampoule of 10ml Water for Injection BP for reconstitution with a sterile disposable syringe (10ml) and a butterfly needle.

Do not use the medicine later than the date of expiry.

Keep all medicines out of the reach of children.

To be dispensed only on the prescription of a registered physician

Manufactured by:
synovia
Synovia Pharma PLC., Station Road, Tongi, Gazipur.
A Subsidiary of BEXIMCO PHARMACEUTICALS LTD.
513960/1

Direction Slip artwork legend

Product Name	:	Carbanem
Code number	:	513960/1
CDCS Version	:	02
Dimension	:	L 13.38 x W 3.75 inches
Min. size of text	:	8 pt
Used Colors	:	Black C ■ Red ■