Only for the use of Medical Professionals

Aronem®

Meropenem

Description

Aronem® IV is the preparation of Meropenem. It is a broad-spectrum carbapenem antibiotic for parenteral use which is active against Gram-positive and Gram- negative bacteria. It is relatively stable to human dehydropeptidase-1 (DHP-1). Meropenem exerts its bactericidal action by interfering with bacterial cell wall synthesis. The basis of the potent bactericidal action of Meropenem against a broad spectrum of aerobic and anaerobic bacteria are ease of penetration into bacterial cell walls, high level of stability to all serine β-lactamases and marked affinity for the Penicillin Binding Proteins (PBPs).

Indications

Aronem® IV is indicated for treatment, in adults and children, of the following infections caused by single or multiple susceptible bacteria sensitive to meropenem:

- Pneumonias including nosocomial pneumonias
- Urinary tract infections
- Intra-abdominal infections
- Gynaecological infections such as endometritis and pelvic inflammatory disease
- Skin and skin structure infections
- Meningitis
- Septicaemia
- Empiric treatment for presumed infections in adult patients with febrile neutropenia used as monotherapy or in combination with anti-viral or anti-fungal agents.

Aronem® IV has proved efficacious alone or in combination with other antimicrobial agents in the treatment of polymicrobial infections.

There is no experience in paediatric patients with neutropenia or primary or secondary immunodeficiency.

Dosage and administration

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. Aronem® should be given as an intravenous bolus injection over approximately 3-5 minutes or by intravenous infusion over approximately 15 to 30 minutes using the specific available presentations.

Adults

The dosage and duration of therapy should be established depending on type and severity of infection and the condition of the patient. The recommended daily dosage of adult is as follows:

- Pneumonias, Urinary tract infections, gynaecological infections such as endometritis and pelvic inflammatory disease; skin and skin structure infections: Aronem® 500 mg IV every 8 hours
- Nosocomial pneumonias, peritonitis, presumed infections in neutropenic patients and septicaemia:
  Aronem® 1 g IV every 8 hours
- Meningitis: Aronem® 2 g IV every 8 hours
- Cystic fibrosis: Aronem® IV up to 2 g every 8 hours

Hepatic impairment: 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.

Patients with impaired renal function: Dosage should be reduced in patients with creatinine clearance < 51 ml/min, as scheduled below:

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

Meropenem is cleared by haemodialysis; 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.

Children

Children 0 to 3 months: Efficacy and tolerability in children under 3 months old have not been established; therefore Meropenem is not recommended.

For children over 3 months to 12 years of age: The recommended dose of Aronem® IV is 10 to 20 mg/kg every 8 hours depending on type and severity of infection, susceptibility of the pathogen and the condition of the patient.

For children aged 4 to 18 years with cystic fibrosis: The doses ranging of Aronem® IV is 25 to 40 mg/kg every 8 hours.

In children 50 kg weight: Adult dosage should be used.

In meningitis: The recommended dose of Aronem® IV is 40 mg/kg every 8 hours.

There is no experience in children with hepatic or renal impairment.

Reconstitution procedure

The content of one vial is to be dissolved in 10 ml water for injection for Aronem® 500mg Iv injection and 20 ml water for injection for Aronem® 1 gm IV injection.

Preparation for injection

Bolus: Aronem® 500mg IV injection vials should be constituted with 10ml sterile water for injections /Aronem® 1g IV injection vials should be constituted with 20ml sterile water for injections (5ml per 250 mg meropenem). This provides an approximate concentration of 50mg/ml. Injection for bolus administration, may be stored for up to 2 hours at controlled room temperature 25°C or for up to **12** hours at 4°C.

Infusion: Aronem® (500 mg and 1g) IV injection vials may be directly constituted with a compatible infusion fluid (50 to 200 ml). Alternatively, an injection vial may be constituted, then the resulting solution added to an IV container and further diluted with an appropriate infusion fluid, as needed.

Compatibility and stability

Aronem® IV is compatible with following infusion fluids: 0.9% Sodium Chloride, 5% or 10% Glucose, 5% Glucose with 0.02% Sodium Bicarbonate, 5% Glucose with 0.9% Sodium Chloride, 5% Glucose with 0.225% Sodium Chloride, 5% Glucose with 0.15% Potassium Chloride and Mannitol 2.5% or 10% solution.

Compatibility of Aronem® IV with other drugs has not been established. Aronem® IV should not be mixed with or physically added to solutions containing other drugs

Freshly prepared solutions of Aronem® IV should be used whenever possible. However constituted solutions of Aronem® IV, as supplied in injection vials, and constituted as noted above, maintain satisfactory potency at room temperature 25 °C or under refrigeration 4°C as shown in the following table:

Diluent	**Hours stable up to**	
	25°C	4°C
Solutions (1 to 20 mg/ml) prepared with:		
a) 0.9% sodium chloride	8	48
b) 5% glucose	3	14
c) 5% glucose and 0.225% sodium chloride	3	14
d) 5% glucose and 0.9% sodium chloride	3	14
e) 5% glucose and 0.15% potassium chloride	3	14
f) 2.5% or 10% mannitol intravenous infusion	3	14
g) 10% glucose	2	8
h) 5% glucose and 0.02% sodium bicarbonate intravenous infusion	2	8

Solutions of Aronem® IV should not be frozen. Shake constituted solution before use. All vials are for single use only. Standard aseptic technique should be employed during constitution and administration.

Pregnancy and lactation

The safety of Meropenem in human pregnancy has not been evaluated. Animal studies have not shown any adverse effect on the developing foetus. Meropenem should not be used in pregnancy unless the potential benefit justifies the potential risk to the foetus. Meropenem is detectable at very low concentrations in animal breast milk. It should be used in lactating women unless the potential benefit justifies the potential risk to the baby.

Side-effects

Meropenem is generally well tolerated. Local injection site reactions, rash, pruritus, urticaria, abdominal pain, nausea, vomiting, diarrhoea, pseudomembranous colitis. Rarely erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis, headache, paraesthesia and infrequently convulsions (although no causal relationship has been established), oral and vaginal candidosis, reversible thrombocythaemia, leucopenia, eosinophilia, thrombocytopenia and neutropenia (including rare cases of agranulocytosis), positive Coombs test, reduction in partial thromboplastin, rarely systemic allergic reactions (hypersensitivity), which may include angioedema and manifestations of anaphylaxis.

Contra-indication

Meropenem is contraindicated in patients who have demonstrated hypersensitivity to this product.

Precautions

Caution in patients with history of hypersensitivity to carbapenems or other β-lactam antibiotics. Before initiating therapy with Meropenem, careful inquiry should be made concerning previous hypersensitivity reactions to β-lactam antibiotics. If an allergic reaction to Meropenem occurs, the drug should be discontinued and appropriate measures should be taken. Monitor transaminase and bilirubin levels when used in hepatic disease. Not recommended for methicillin-resistant staphylococci infections. Monitor for overgrowth of non-susceptible organisms. In patients who develop diarrhoea, consider diagnosis of pseudomembranous colitis. Caution in individuals with a history of gastro-intestinal complaints, particularly colitis. Caution if to be co-administered with potentially nephrotoxic drugs. Co-administration with probenicid not recommended. Meronem may reduce serum valproic acid levels, sub-therapeutic levels may occur. No specific drug interaction data are available. Caution when used as monotherapy for known or suspected *Pseudomonas aeruginosa* lower respiratory tract infections, regular sensitivity testing is recommended.

Overdosage

Accidental overdosage could occur during therapy, particularly in patients with renal impairment. Treatment of accidental overdosage should be symptomatic. In normal individuals, rapid renal elimination will occur; in subjects with renal impairment, haemodialysis will remove Meropenem and its metabolite.

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. Therefore, co-administration of Probenecid with Meropenem is not recommended. Meropenem may reduce serum valproic acid levels. Subtherapeutic levels may be reached in some patients.

Pharmaceutical precautions

Store in a cool and dry place (below 30^0 C). It is recommended to use freshly prepared solutions of Aronem® for IV injection and infusion. Reconstituted product should be used immediately and must be stored for no longer than 24 hours under refrigeration, only if necessary.

Presentation

Aronem® 500 mg IV injection: Each vial contains Meropenem USP 500 mg.
Aronem® 1 g IV injection: Each vial contains Meropenem USP 1 g.

Package quantities

Aronem® 500 mg IV injection: Carton containing one vial of Aronem® 500 mg sterile powder, one ampoule of 10 ml water for injection BP, a disposable syringe (10 ml/cc), a butterfly needle, a first aid bandage and an alcohol pad.
Aronem® 1 g IV injection: Carton containing one vial of Aronem® 1 g sterile powder, two ampoules of 10 ml water for injection BP, a disposable syringe (20 ml/cc), a butterfly needle, a first aid bandage and an alcohol pad.

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