Ronem®

Meropenem

Description: Meropenem (**Ronem®**) is a broad spectrum ß-lactam antibacterial agent of the carbapenem class. Like other ß-lactam antibiotic, it is bactericidal in action exerting its effect by inhibiting transpeptidase enzyme responsible for cell-wall synthesis. It has a very broad spectrum of activity, including activity against Gram-positive and Gram-negative aerobic and anaerobic organisms, and is stable to hydrolysis by beta-lactamases enzyme produced by most bacterial species. Meropenem is more stable to renal dehydropeptidase-I than Imipenem/Cilastatin.

Mode of action: Meropenem (**Ronem®**) inhibits bacterial cell wall synthesis and thus exerts bactericidal action.

Pharmacokinetics: Following intravenous injection of Meropenem 500 mg and 1g over 5 minutes, peak plasma concentrations of about 50 and 112 μg/mL respectively are attained. The same doses infused over 30 minutes produce peak plasma concentrations of about 23 and 49 μg/mL, respectively. Meropenem has a plasma elimination half-life of about 1 hour; this may be prolonged in patients with renal impairment and is also slightly prolonged in children. Meropenem is widely distributed into body tissues and fluids including the CSF and bile. It is more stable to renal dehydropeptidase-I than Imipenem and mainly excreted by urine, by tubular secretion and glomerular filtration. About 70% of a dose is recovered unchanged in the urine over a 12-hour period and urinary concentrations above 10 μg/mL are maintained for upto 5 hours after a 500 mg dose. Meropenem has one reactive metabolite which is excreted in the urine. Meropenem is removed by haemodialysis.

Composition: Ronem® 500 mg Injection: Each vial contains sterile Meropenem Trihydrate USP 570 mg equivalent to sterile Meropenem 500 mg.
Ronem® 1g Injection: Each vial contains sterile Meropenem Trihydrate USP 1.14 gm equivalent to sterile Meropenem 1 gm.

Indications: Ronem® is indicated for the treatment of following indications caused by single or multiple bacteria sensitive to Meropenem and as empiric therapy prior to the identification of causative organisms. Intra-abdominal sepsis, deep gynecological and obstetric infections, septicemia of unknown etiology, meningitis, pulmonary infections in cystic fibrosis patients, febrile neutropenia, pneumonia, urinary tract infections, and skin and skin structure infections.

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. Usual adult dose is 500 mg to 1g by intravenous administration every 8 hours. Meropenem should be given by intravenous infusion, over approximately 15 to 30 minutes or as an intravenous bolus injection (5 to 20 mL) over approximately 3-5 minutes.

Indication wise recommended daily dosage is as follows:

- 500 mg IV every 8 hours in the treatment of pneumonia, UTI, gynecological infection such as endometritis, skin and skin structure infections.
- 1 g IV every 8 hours in the treatment of nosocomial pneumonia, peritonitis, presumed infection in neutropenic patients, septicemia.
- In meningitis the recommended daily dosage is 2 g every 8 hours.

Dosage schedule for Adults with Renal Impairment: Dosage should be reduced in patients with creatinine clearance less than 51 mL/min.

Recommended Dosage Schedule:

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

Dosage for Adults with Hepatic Insufficiency: No dosage adjustment is necessary in patients with impaired hepatic function.

Dosage for Elderly Patients: No dosage adjustment is required for elderly patients with creatinine clearance greater than 50 mL/min.

Dosage for Paediatric Patients: For paediatric patients from 3 months to 12 years of age, Meropenem dose is 20 or 40 mg/kg every 8 hours (maximum dose is 2 g every 8 hours), depending on the type of infection (intra-abdominal or meningitis). Paediatric patients weighing over 50 kg should be administered Meropenem at a dose of 1 g every 8 hours for intra-abdominal infections and 2 g every 8 hours for meningitis.

Recommended Dosage Schedule for Paediatric Patients with Normal Renal Function:

Type of infection	Dose (mg/kg)	Dosing interval
Intra-abdominal infection	20	Every 8 hours
Meningitis	40	Every 8 hours

Instruction for use: For Intravenous bolus administration, constitute injection vials (500 mg and 1 g) with sterile Water for Injection. Shake to dissolve and let stand until clear. Freshly constituted solutions are clear, and colorless or pale yellow.

Strength	Amount of diluent to be added (mL)	Approximate withdrawable volume (mL)	Approximate withdrawable concentration (mg/mL)
500 mg	10	10	50
1 g	20	20	50

Infusion vial (1 g injection) may be directly constituted with a compatible infusion fluid. Alternatively, an injection vial may be constituted, then the resulting solution is added to an IV container and further diluted with an appropriate infusion fluid. For IV administration, Meropenem is compatible at concentration between 1 and 20 mg/mL with appropriate diluents.

Compatible diluents and Storage after reconstitution: **Ronem®** is compatible with the following infusion fluids and freshly prepared solution of it (for IV injection and infusion) maintains satisfactory potency at room temperature (upto 25 ˚C) or under refrigeration (4 ˚C) as shown in the following table:

Diluent	Hours stable at 15 ~ 25ºC	Hours stable at 4ºC
Vials constituted with Water for Injections for bolus Injection	8	48
Solutions (1~20 mg/mL) prepared with:		
• 0.9% Sodium chloride	8	48
• 5% Glucose	3	14
• 5% Glucose and 0.225% Sodium chloride	3	14
• 5% Glucose and 0.9% Sodium chloride	3	14
• 5% Glucose and 0.15% Potassium chloride	3	14
• 2.5% or 10% mannitol intravenous infusion	3	14
• 10% Glucose	2	8
• 5% Glucose and 0.02% Sodium bicarbonate intravenous infusion	2	8

Contraindications: Meropenem is contraindicated in patients with known hypersensitivity to any component of it or to other drugs in the same class or in patients who have demonstrated anaphylactic reactions to ß-lactams.

Side effects: Nausea, vomiting, diarrhoea (antibiotic-associated colitis reported), abdominal pain; disturbances in liver function tests; thrombocytopenia (reduction in partial thromboplastin time reported), positive Coombs' test, eosinophilia, leucopenia, neutropenia; headache, paraesthesia; hypersensitivity reactions including rash, pruritus, urticaria, angioedema, and anaphylaxis; also reported convulsions, Stevens-Johnson syndrome and toxic epidermal necrolysis; local reactions including pain and thrombophlebitis at injection site.

Use in pregnancy and lactation: There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Meropenem is administered to a nursing woman.

Precautions: It should not be given to patients who are hypersensitive to it or other penicillins, cephalosporins or other ß-lactams because of the possibility of cross-sensitivity. It should be given with caution to patients with renal impairment: a dosage reduction may be necessary.

Drug interactions: *Probenecid:* Excretion of Meropenem is reduced by probenecid (avoid concomitant use). *Valproate:* Meropenem reduces plasma concentration of valproate. *Oestrogens:* Broad-spectrum antibacterials possibly reduce contraceptive effect of oestrogens.

Over dosage: Intentional overdosing of Meropenem is unlikely, although accidental overdosing might occur if large doses are given to patients with reduced renal function. The largest dose of Meropenem administered in clinical trials has been 2 g given intravenously every 8 hours. At this dosage, no adverse pharmacological effects or increased safety risks have been observed. No specific information is available for the treatment of Meropenem overdosage. In the event of an overdose, Meropenem should be discontinued and general supportive treatment given until renal elimination takes place. Meropenem and its metabolite are readily dialyzable and effectively removed by hemodialysis; however, no information is available on the use of hemodialysis to treat overdosage.

Storage: Store in a cool and dry place, protected from light.

Packaging:
Ronem® 500 mg Injection: Each carton contains one vial with one ampoule of 10 ml sterile Water for Injection in a blister pack and a 10 ml disposable syringe.
Ronem® 1g Injection: Each carton contains one vial with two ampoules of 10 ml sterile Water for Injection, a 20 ml disposable syringe, a first aid bandage and an alcohol pad.

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Ideas for healthcare

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