OLVER® I.V. 500mg 1g

(Meropenem as Trihydrate)
For Injection U.S.P

اولور ۵۰۰ ملی گرام ۱ گرام انجکشن یو ایس پی
(میروپینم بطور ٹرائی ہائیڈریٹ)
صرف ہسپتال استعمال کیلئے

QUALITATIVE AND QUANTITATIVE COMPOSITION

Meropenem (as Trihydrate) U.S.P.....500mg also contains 45.1mg sodium as sodium carbonate (1.96 mEq).

Meropenem (as Trihydrate) U.S.P. .....1g also contains 90.2mg sodium as sodium carbonate (3.92 mEq).

DESCRIPTION

OLVER I.V. is a white to pale yellow crystalline powder. The solution varies from colorless to yellow depending on the concentration. The pH of freshly constituted solutions is between 7.3 and 8.3.

CLINICAL PHARMACOLOGY

Mechanism of action: Meropenem is an antibacterial drug. The bactericidal activity of meropenem results from the inhibition of cell wall synthesis. Meropenem penetrates the cell wall of most gram-positive and gram-negative bacteria to reach penicillin-binding-protein (PBP) targets. Meropenem binds to PBPs 2, 3 and 4 of Escherichia coli and Pseudomonas aeruginosa; and PBPs 1, 2 and 4 of Staphylococcus aureus. Bactericidal concentrations (defined as a 3 log10 reduction in cell counts within 12 hours to 24 hours) are typically 1-2 times the bacteriostatic concentrations of meropenem, with the exception of Listeria monocytogenes, against which lethal activity is not observed. Meropenem has significant stability to hydrolysis by β-lactamases, both penicillinases and cephalosporinases produced by gram-positive and gram-negative bacteria. **Pharmacokinetics: Plasma concentration:** At the end of a 30-minute intravenous infusion of a single dose of OLVER I.V. in healthy volunteers, mean peak plasma concentrations of meropenem are approximately 23 mcg/mL (range 14-26) for the 500mg dose and 49 mcg/mL (range 39-58) for the 1 gram dose. No accumulation of meropenem in plasma was observed with regimens using 500mg administered every 8 hours or 1g administered every 6 hours in healthy volunteers with normal renal function. **Distribution:** The plasma protein binding of meropenem is approximately 2%. **Metabolism:** There is one metabolite of meropenem that is microbiologically inactive. **Excretion:** Meropenem is primarily excreted unchanged by the kidneys. Approximately 70% (50% – 75%) of the dose is excreted unchanged within 12 hours.

INDICATIONS AND USAGE

Meropenem is indicated for the treatment of the following infections in adults and children over 3 months of age • Aerobic and anaerobic Gram-positive and Gram-negative infections • Severe pneumonia, including hospital and ventilator-associated pneumonia • Broncho-pulmonary infections in cystic fibrosis • Complicated urinary tract infections • Complicated intra-abdominal infections • Intra-and post-partum infections • Acute bacterial meningitis • Complicated skin and skin structure infections • Treatment of patients with bacteraemia.

Meropenem may be used in the management of neutropenic patients with fever that is suspected to be due to a bacterial infection. To reduce the development of drug-resistant bacteria and maintain the effectiveness of OLVER I.V. and other antibacterial drugs, OLVER I.V. should only be used to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

CONTRAINDICATIONS

OLVER I.V. is contraindicated in patients with known hypersensitivity to any component of this product or to other drugs in the same class or in patients who have demonstrated anaphylactic reactions to beta (β)- lactams.

INTERACTIONS

Co-administration of OLVER I.V. with probenecid inhibits renal excretion of meropenem and is therefore not recommended).

• The concomitant use of OLVER I.V. and valproic acid or divalproex sodium is generally not recommended. Anti-bacterial drugs other than carbapenems should be considered to treat infections in patients whose seizures are well controlled on valproic acid or divalproex sodium.

USE IN SPECIFIC POPULATION

Geriatric Use: Meropenem is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with renal impairment.

Pediatric Use: The safety and effectiveness of OLVER I.V. have been established for pediatric patients 3 months of age and older with complicated skin and skin structure infections and bacterial meningitis, and for pediatric patients of all ages with complicated intra-abdominal infections. **Patients with Renal Impairment:** Dosage adjustment is necessary in patients with creatinine clearance 50 mL/min or less. **Pregnancy: Category B.** There are no adequate and well-controlled studies with meropenem in pregnant women. **Nursing Mothers:** Meropenem has been reported to be excreted in human milk. Caution should be exercised when OLVER I.V. is administered to a nursing woman. **Patients with hepatic Impairment:** A pharmacokinetic study with OLVER I.V. in patients with hepatic impairment has shown no effects of liver disease on the pharmacokinetics of meropenem.

PRECAUTIONS

Hypersensitivity Reactions: Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving therapy with β-lactams. **Seizure Potential:** Seizures and other adverse CNS experiences have been reported during treatment with OLVER I.V. **Risk of Breakthrough Seizures Due to Drug Interaction with Valproic Acid:** The concomitant use of meropenem and valproic acid or divalproex sodium is generally not recommended. **Clostridium difficile–associated Diarrhea:** Clostridium difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including I.V. and may range in severity from mild diarrhea to fatal colitis. **Development of Drug-Resistant Bacteria:** Prescribing OLVER I.V. in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria. **Overgrowth of Nonsusceptible Organisms:** As with other broad-spectrum antibacterial drugs, prolonged use of meropenem may result in overgrowth of nonsusceptible organisms. **Thrombocytopenia:** In patients with renal impairment, thrombocytopenia has been observed but no clinical bleeding reported. **Potential for Neuromotor Impairment:** Alert patients receiving OLVER I.V. on an outpatient basis regarding adverse events such as seizures, delirium, headache and/or paresthesia that could interfere with mental alertness and/or cause motor impairment.

ADVERSE REACTIONS

Inflammation at the injection site, Phlebitis/thrombophlebitis, Pain at the injection site, Edema at the injection site Diarrhea, nausea/vomiting, headache, rash , sepsis, constipation, apnea, shock, and pruritus. Gastrointestinal hemorrhage, melena, epistaxis, hemoperitoneum. **Body as a Whole:** Pain, abdominal pain, chest pain, fever, back pain, abdominal enlargement, chills, pelvic pain. **Cardiovascular:** Heart failure, heart arrest, tachycardia, hypertension, myocardial infarction, pulmonary embolus, bradycardia, hypotension, syncope. Oral moniliasis, anorexia, cholestatic jaundice/jaundice, flatulence, ileus, hepatic failure, dyspepsia, intestinal obstruction Hemic/Lymphatic: Anemia, hypochromic anemia, hypervolemia. **Metabolic/Nutritional:** Peripheral edema, hypoxia. **Nervous System:** Insomnia, agitation, delirium, confusion, dizziness, seizure, nervousness, paresthesia, hallucinations, somnolence, anxiety, depression. **Respiratory:** Respiratory disorder, dyspnea, pleural effusion, asthma, cough increased, lung edema. **Skin and Appendages:** Urticaria, sweating, skin ulcer. **Urogenital System:** Dysuria, kidney failure, vaginal moniliasis, urinary incontinence. **Hepatic:** Increased alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase, lactate dehydrogenase (LDH), and bilirubin. **Hematologic:** Increased platelets, increased eosinophils, decreased platelets, decreased hemoglobin, decreased hematocrit, decreased white blood cell (WBC), shortened prothrombin time and shortened partial thromboplastin time, leukocytosis, hypokalemia. **Renal:** Increased creatinine and increased blood urea nitrogen (BUN). **Urinalysis:** Presence of red blood cells. **Sideffects:** Headache, nausea, constipation, diarrhea, anemia, vomiting, and rash.

DOSAGE AND ADMINISTRATION

500 mg every 8 hours by intravenous infusion over 15 to 30 minutes for complicated skin and skin structure infections (cSSSI) for adult patients. When treating, infections caused by Pseudomonas aeruginosa, a dose of 1 gram every 8 hours is recommended. 1 gram every 8 hours by intravenous infusion over 15 minutes to 30 minutes for intra-abdominal infections for adult patients. 1 gram every 8 hours by intravenous bolus injection (5 mL to 20 mL) over 3 minutes to 5 minutes for adult patients. Dosage should be reduced in adult patients with renal impairment. 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 infections due to less susceptible bacterial species (e.g. Enterobacteriaceae, Pseudomonas aeruginosa, Acinetobacter spp.), or very severe infections.

Adults and Adolescents

Infection	Dose to be administered every 8 hours
Severe pneumonia including hospital and ventilator-associated pneumonia.	500 mg or 1 g
Broncho-pulmonary infections in cystic fibrosis	2 g
Complicated urinary tract infections	500 mg or 1 g
Complicated intra-abdominal infections	500 mg or 1 g
Intra- and post-partum infections	500 mg or 1 g
Complicated skin and soft tissue infections	500 mg or 1 g
Acute bacterial meningitis	2 g
Management of febrile neutropenic patients	1 g

Meropenem is usually given by intravenous infusion over approximately 15 to 30 minutes. Alternatively, doses up to 1 g can be given as an intravenous bolus injection over approximately 5 minutes. There are limited safety data available to support the administration of a 2g dose in adults as an intravenous bolus injection.

Renal impairment patient: Dosage should be reduced in patients with creatinine clearance of 50 mL/min or less. Recommended OLVER I.V. Dosage Schedule for Adult Patients with Renal Impairment.

Creatinine Clearance (mL/min)	Dose (dependent on type of infection)	Dosing Interval
Greater than 50	Recommended dose (500 mg cSSSI and 1 gram Intra-abdominal)	Every 8 hours
26-50	Recommended dose	Every 12 hours
10-25	One-half recommended dose	Every 12 hours
Less than 10	One-half recommended dose	Every 24 hours

There is inadequate information regarding the use of OLVER I.V. in patients on hemodialysis or peritoneal dialysis.

Pediatric patients 3 months of age and older

Recommended OLVER IV Dosage Schedule for Pediatric Patients 3 Months of Age and Older with Normal Renal Function (upto 50kg body weight)			
Type of Infection	**Dose (mg/kg)**	**Up to a Maximum Dose**	**Dosing Interval**
Complicated skin and skin structure*	10	500 mg	Every 8 hours
Intra-abdominal	20	1 gram	Every 8 hours
Meningitis	40	2 gram	Every 8 hours

Intravenous infusion is to be given over approximately 15 minutes to 30 minutes.
- Intravenous bolus injection (5 mL to 20 mL) is to be given over approximately 3 minutes-5 minutes.
*20 mg/kg (or 1 gram for pediatric patients weighing over 50 kg) every 8 hours is recommended when treating complicated skin and skin structure infections caused by P. aeruginosa.
In severe pneumonia including hospital and ventilator-associated pneumonia, 10 or 20mg/kg, Broncho-pulmonary infections in cystic fibrosis,40mg/kg ,complicated urinary tract infections,10 or20mg/kg and for management of febrile neutropenic patients,20mg/kg every 8hours.
For children over 50kg body weight, adult dose should be administered.

Pediatric patients less than 3 months of age

Recommended OLVER IV Dosage Schedule for Pediatric Patients Less than 3 Months of Age with Complicated Intra-Abdominal Infections and Normal Renal Function		
Age Group	**Dose (mg/kg)**	**Dose Interval**
Infants less than 32 weeks GA and PNA less than 2 weeks	20	Every 12 hours
Infants less than 32 weeks GA and PNA 2 weeks and older	20	Every 8 hours
Infants 32 weeks and older GA and PNA less than 2 weeks	20	Every 8 hours
Infants 32 weeks and older GA and PNA 2 weeks and older	30	Every 8 hours

- Intravenous infusion is to be given over 30 minutes.
- There is no experience in pediatric patients with renal impairment.
GA: gestational age and PNA: postnatal age

Preparation and Administration of OLVER I.V.

Important Administration Instructions:

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

For Intravenous Bolus Administration

Re-constitute injection vials (500mg and 1g) with sterile Water for Injection.

Shake to dissolve and let stand until clear.

Volume of Sterile Water for Injection for Reconstitution of Injection Vials

Vial Size	Amount of Diluent Added (mL)	Approximate Withdrawable Volume (mL)	Approximate Average Concentration (mg/mL)
500 mg	10	10	50
1 gram	20	20	50

Compatibility: Compatibility of OLVER I.V. with other drugs has not been established. OLVER I.V. should not be mixed with or physically added to solutions containing other drugs.

Intravenous Infusion Administration: For intravenous infusion meropenem vials may be directly constituted with 0.9 % sodium chloride or 5% glucose (dextrose) solutions for infusion to a final concentration of 1 to 20mg/ml.

Intravenous Bolus Administration: OLVER I.V. injection vials re-constituted with sterile Water for Injection for bolus administration (up to 50mg/mL of OLVER I.V.).

INSTRUCTIONS:

Dosage as directed by the physician. Store at 25°C, excursions permitted to 15°C to 30°C, Do not freeze. Protect from sunlight and moisture. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only solutions prepared for infusion concentrations ranging from 1mg/mL to 20mg/mL re-constituted with Dextrose Injection 5% should be used immediately.

AFTER RECONSTITUTION:

Intravenous bolus: May be stored for 3-hours at 25°C or for 13-hours at 5°C.

Intravenous Infusion: May be stored for 1-hours at 25°C or for 15-hours at 5°C (if reconstituted with 0.9% sodium chloride). Intravenious Infusion reconstituted with dextrose injection should be use immediately. Not to be used if solution is not clear. Sterile mixture also contains sodium carbonate as buffer.

PRESENTATION

OLVER I.V. (Meropenem as Trihydrate) 500mg injection U.S.P. is available in pack of 1vial+10ml sterile Water for Injection.

OLVER I.V. (Meropenem as Trihydrate) 1g injection U.S.P. is available in pack of 1vial+20ml sterile Water for Injection.

ہدایات: خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

۲۵ ڈگری سینٹی گریڈ پر رکھیں، محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔

روشنی اور نمی سے محفوظ رکھیں۔

دوا کی تیاری کے بعد: ۲۴ گھنٹے کمرے کے درجہ حرارت پر محفوظ رکھا جا سکتا ہے۔

انجکشن کے لیک ہونے، دُھندلا ہونے یا اس میں کوئی غیر حل پذیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔ غیر استعمال شدہ سلوشن کو ضائع کر دیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

For detailed information please contact.

Genix Pharma (Pvt.) Ltd.

44,45-B, Korangi Creek Road, Karachi-75190, Pakistan.

UAN: +92-21-111-10-10-11, **Email:** info@genixpharma.com

ISO 9001:2015 ISO 14001:2015 ISO 45001:2018

www.genixpharma.com