ALEEVA®
(Cefepime)
For Injection U.S.P.

500mg, 1g/vial
For I.V./I.M. use
after reconstitution

الیوا
(سیفیپائیم)
۵۰۰ ملی گرام، ۱ گرام
انجکشن یو۔ایس۔پی
عضلاتی/وریدی استعمال کیلئے

QUALITATIVE AND QUANTITATIVE COMPOSITION
Aleeva For Injection U.S.P 500mg
Each vial contains: Cefepime hydrochloride equivalent to 500mg Cefepime (with L-Arginine).
Aleeva For Injection U.S.P. 1g
Each vial contains: Cefepime hydrochloride equivalent to 1g Cefepime (with L-Arginine).

DESCRIPTION
ALEEVA (Cefepime Hydrochloride, U.S.P) is a semi-synthetic, cephalosporin antibacterial for parenteral administration. Aleeva is a sterile, dry mixture of cefepime hydrochloride and L-arginine. The L-arginine, at an approximate concentration of 707 mg/g of cefepime, is added to control the pH of the constituted solution at 4 to 6.

CLINICAL PHARMACOLOGY
Mechanism of Action: Cefepime is a cephalosporin antibacterial drug inhibits the cell wall synthesis. **Pharmacokinetics:** Elimination of cefepime is principally via renal excretion with an average (±SD) half-life of 2 (±0.3) hours and total body clearance of 120 (±8) mL/min in healthy volunteers. Cefepime pharmacokinetics are linear. **Absorption:** Following intramuscular (IM) administration, cefepime is completely absorbed. **Distribution:** The average steady-state volume of distribution of cefepime is 18 (±2) L. **Metabolism and Excretion:** Cefepime is metabolized to N-methylpyrrolidine (NMP) which is rapidly converted to the N-oxide (NMP-N-oxide).

INDICATIONS AND USAGE
Pneumonia, Febrile Neutropenic Patients, uncomplicated and complicated urinary tract infections (including pyelonephritis), Uncomplicated Skin and Skin Structure Infections, Complicated Intra-Abdominal Infections (used in combination with metronidazole).

CONTRAINDICATIONS
ALEEVA is contraindicated in patients who have shown immediate hypersensitivity reactions to cefepime or the cephalosporin class of antibiotics, penicillins or other beta-lactam antibiotics.

INTERACTIONS
Drug/Laboratory Test Interactions: The administration of cefepime may result in a false-positive reaction for glucose in the urine with certain methods. Aminoglycosides: Monitor renal function if aminoglycosides are to be administered with ALEEVA. **Diuretics:** Nephrotoxicity has been reported following concomitant administration of other cephalosporins with potent diuretics such as furosemide.

USE IN SPECIFIC POPULATION
Pregnancy Category B: There are no adequate and well-controlled studies of cefepime use in pregnant women. **Nursing Mothers:** Cefepime is excreted in human breast milk. Caution should be exercised. **Pediatric Use:** The safety and effectiveness of cefepime have been established in the age groups 2 months up to 16 years. Safety and effectiveness in pediatric patients below the age of 2 months have not been established. **Geriatric Use:** Serious adverse events have occurred in geriatric patients with renal insufficiency given unadjusted doses of cefepime, including life threatening or fatal occurrences of the following: encephalopathy, myoclonus, and seizures. **Renal Impairment:** Adjust the dose of ALEEVA in patients with creatinine clearance less than or equal to 60 mL/min to compensate for the slower rate of renal elimination. **Hepatic Impairment:** No dose adjustment is necessary for patients with impaired hepatic function.

PRECAUTIONS
Hypersensitivity Reactions: Patient should be checked for hypersensitivity reactions to cefepime, cephalosporins, penicillins, or other beta-lactams before start of therapy.
Neurotoxicity: Encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), aphasia, myoclonus, seizures, and nonconvulsive status. **Clostridium difficile Associated Diarrhea:** Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including ALEEVA, and may range in severity from mild diarrhea to fatal colitis. **Development of Drug-Resistant Bacteria:** Prolonged use of ALEEVA may result in overgrowth of nonsusceptible microorganisms. Ability to perform tasks that require judgment, motor or cognitive skills: Caution is necessary as cefepime cause dizziness and disturbance of consciousness.

ADVERSE REACTIONS
Hypersensitivity Reactions, Neurotoxicity and Clostridium difficile-Associated Diarrhea. Cephalosporin-Class Adverse Reactions: Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, renal dysfunction, toxic nephropathy, aplastic anemia, hemolytic anemia, hemorrhage, hepatic dysfunction including cholestasis, and pancytopenia. **Side effects:** Fever, headache, nausea, vomiting, anemia, phlebitis, pain and/or inflammation, rash, pruritus.

DOSAGE AND ADMINISTRATION
Dosage for Adults: Administer ALEEVA intravenously over approximately 30 minutes. The recommended adult dosages and routes of administration for patients with creatinine clearance, greater than 60mL/min are as follows:

Recommended Dosage Schedule for ALEEVA in Adult Patients with Creatinine Clearance (CrCL) Greater Than 60 mL/min

Site and Type of Infection	Dose	Frequency	Duration(days)
Adults	Intravenous (IV)/ Intramuscular (IM)		
Moderate to Severe Pneumonia	1 to 2 g IV	Every 8 to 12 hours	10
Empiric therapy for febrile neutropenic patients	2 g IV	Every 8 hours	7*
Mild to Moderate Uncomplicated or Complicated Urinary Tract Infections, including pyelonephritis	0.5 to 1 g IV/IM**	Every 12 hours	7 to 10
Severe Uncomplicated or Complicated Urinary Tract Infections, including pyelonephritis	2 g IV	Every 12 hours	10
Moderate to Severe Uncomplicated Skin and Skin Structure Infections	2 g IV	Every 12 hours	10
Complicated Intra-abdominal Infections §(used in combination with metronidazole)	2 g IV	Every 8 to 12 hours	7 to 10

*or until resolution of neutropenia. In patients, whose fever resolves but who remain neutropenic for more than 7 days, the need for continued antimicrobial therapy should be re-evaluated frequently. **Intramuscular route of administration is indicated only for mild to moderate, uncomplicated or complicated UTIs due to E. coli. §For P. aeruginosa, use 2 g IV every 8 hours. Pediatric Patients (2 months up to 16 years): The maximum dose for pediatric patients should not exceed the recommended adult dose. The usual recommended dosage in pediatric patients up to 40 kg in weight for durations as given above for adults is:

•50 mg per kg per dose, administered every 12 hours for uncomplicated and complicated urinary tract infections (including pyelonephritis), uncomplicated skin and skin structure infections, and pneumonia. •For

moderate to severe pneumonia due to P. aeruginosa give 50mg per kg per dose, every 8 hours. •50mg per kg per dose, every 8 hours for febrile neutropenic patients. Dosage Adjustments in Patients with Renal Impairment: Adult Patients Adjust the dose of ALEEVA in patients with creatinine clearance less than or equal to 60 mL/min to compensate for the slower rate of renal elimination. In these patients, the recommended initial dose of ALEEVA should be the same as in patients with CrCL greater than 60 mL/min except in patients undergoing hemodialysis. The recommended doses of ALEEVA in patients with renal impairment are presented are as follows:

Recommended Dosing Schedule for ALEEVA in Adult Patients With Creatinine Clearance Less Than or Equal to 60mL/min				
Creatinine Clearance (mL/min)	**Recommended Maintenance Schedule**			
Greater than 60	500 mg every 12 hours	1 g every 12 hours	2 g every 12 hours	2 g every 8 hours
30 to 60	500 mg every 24 hours	1 g every 24 hours	2 g every 24 hours	2 g every 12 hours
11 to 29	500 mg every 24 hours	500 mg every24 hours	1 g every 24 hours	2 g every 24 hours
Less than 11	250 mg every 24 hours	250 mg every 24 hours	500 mg every 24hours	1g every 24 hours
Continuous Ambulatory Peritoneal Dialysis (CAPD)	500 mg every 48 hours	1 g every 48 hours	2 g every 48 hours	2 g every 48 hours
Hemodialysis*	1 g on day 1, then 500 mg every 24 hours thereafter			1 g every 24 hours

*On hemodialysis days, cefepime should be administered following hemodialysis. Whenever possible, cefepime should be administered at the same time each day. In patients undergoing Continuous Ambulatory Peritoneal Dialysis (CAPD), ALEEVA may be administered at the recommended doses at a dosage interval of every 48 hours. In patients undergoing hemodialysis, approximately 68% of the total amount of cefepime present in the body at the start of dialysis will be removed during a 3-hour dialysis period. The dosage of ALEEVA for hemodialysis patients is 1 g on Day 1 followed by 500 mg every 24 hours for the treatment of all infections except febrile neutropenia, which is 1 g every 24 hours. ALEEVA should be administered at the same time each day and following the completion of hemodialysis on hemodialysis days.

Preparation of ALEEVA for Intravenous Infusion

Constitute the 0.5 gram and 1 gram vial, of ALEEVA with the one of the following diluents:

Sterile Water for Injection, 0.9% Sodium Chloride Injection, 5% Dextrose Injection, 0.5% or 1% Lidocaine Hydrochloride Injection, Sterile Bacteriostatic Water for Injection with Parabens or Benzyl Alcohol.

Dilute the reconstituted solution with one of the following compatible infusion solutions prior to intravenous infusion

- 0.9% Sodium Chloride Injection
- 5% and 10% Dextrose Injection
- M/6 Sodium Lactate Injection
- 5% Dextrose and 0.9% sodium Chloride Injection
- Lactated Rings and 5% Dextrose Injection
- Normosol™-R and Normosol™-M in 5% Dextrose Injection
- Dilute with compatible diluent to 50ml or 100ml
- Administer the resulting intravenous infusion over approximately 30 minutes.
- Intermittent intravenous infusion with a Y-type administration set can be accomplished with compatible solutions. However, during infusion of a solution containing cefepime, it is desirable to discontinue the other solution.

Preparation of ALEEVA for Intramuscular Administration

Constitute ALEEVA vials 0.5 gram, 1 gram with one of the following diluents: Sterile Water for Injection, 0.9% Sodium Chloride, 5% Dextrose Injection, 0.5% or 1% Lidocaine Hydrochloride, or Sterile Bacteriostatic Water for Injection with Parabens or Benzyl Alcohol. Parenteral drugs should be inspected visually for particulate matter before administration. If particulate matter is evident in reconstituted fluids, the drug solution should be discarded.

Preparation of Reconstituted Solutions of ALEEVA for Injection:

Single-Dose Vials for Intravenous (IV)/Intramuscular (1M)Administration	Amount of Diluent to be added mL	Approximate Cefepime Concentration m /mL	Amount of Reconstituted Volume to be Withdrawn mL
Cefepime vial content			
500 mg (IV)	5	100	5
500 mg (1M)	1.5	280	1.8
1 g (IV)	10	100	10.5
1 g (1M)	3	280	3.6
2 g (IV)	10	160	12.5

Intramuscular and Intravenous ALEEVA

As with other cephalosporins, the color of ALEEVA powder, as well as its solutions tend to darken depending on storage conditions; however, when stored as recommended, the product potency is not adversely affected.

INSTRUCTIONS:

Dosage as directed by the physician. Store at 20°C-25°C, excursions permitted to 15°C-30°C. Protect from sunlight & moisture.

Reconstitute before intramuscular use. Dilute before Intravenous Infusion. Keep all medicines out of the reach of children. Injection should not be used if container is leaking, solution is cloudy or it contains un-dissolved particles.

STORAGE OF RECONSTITUTED SOLUTION:

Reconstituted solution should be stored up to 24 hours at controlled room temperature 20°C to 25°C or 7 days in a refrigerator 2°C to 8°C.

WARNING: To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

ALEEVA (Cefepime Hydrochloride) 500mg For Injection U.S.P. is available as 1 glass vial packed along with 1 ampoule of 5mL water for Injection and insert.

ALEEVA (Cefepime Hydrochloride) 1g For Injection U.S.P. is available as 1 glass vial packed along with 1 ampoule of 10mL water for Injection and insert.

علامات/طریقہ استعمال :

الیوا مندرجہ ذیل علامات میں تجویز کردہ ہے۔نمونیہ، فبرائل نیوٹروپینیا، گردے، جلد اور معدے سے منسلک امراض۔

الیوا انجکشن انٹراوینسلی ۳۰ منٹ کے دورانیہ میں استعمال کریں۔مختلف امراض کے لحاظ سے خوراک ڈاکٹر کی ہدایت کے مطابق تجویز کردہ ہے۔ گردے کے مریضوں میں خوراک کو کریٹینین کلیرنس کے لحاظ سے ترتیب دیا جاتا ہے۔

عمومی خوراک : بڑوں کے لئے: ۱ یا ۲ گرام دن میں ۲ سے ۳ مرتبہ۔
بچوں کے لئے : ۵۰ ملی گرام / کلوگرام دن میں ۲ سے ۳ مرتبہ۔

دوا کی تیاری:

انٹرامسکلر استعمال کے لئے: ۵۰۰ ملی گرام کی وائل میں ۱.۵ ملی لیٹر واٹر فار انجکشن اور ۱ گرام کی وائل میں ۳ ملی لیٹر واٹر فار انجکشن شامل کریں۔

انٹراوینس استعمال کے لئے: ۵۰۰ ملی گرام کی وائل میں ۵ ملی لیٹر واٹر فار انجکشن اور ۱ گرام کی وائل میں ۱۰ ملی لیٹر واٹر فار انجکشن شامل کریں۔

تیار شدہ محلول کو ۲۰ سے ۲۵ ڈگری سینٹی گریڈ پر ۲۴ گھنٹے تک رکھا جاسکتا ہے۔
اور ۲ سے ۸ ڈگری سینٹی گریڈ پر ۷ دن تک رکھا جاسکتا ہے۔

مضر اثرات: بخار، سردرد، متلی، اُلٹی، خون کی کمی، ورید کی سوزش، درد، سوزش، خارش، پرورائٹس۔ نیوروٹوکسیٹی، کلوسٹریڈم ڈفیسائل سے مشروط دست، مزاحمتی بیکٹیریا کی پیداوار میں اضافہ ہونے کا خدشہ ہے۔

احتیاطی تدابیر: علاج شروع کرنے سے پہلے حساس مریضوں کی تشخیص لازمی ہے۔

ہدایات: خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔ ۲۰ سے ۲۵ ڈگری سینٹی گریڈ پر رکھیں، محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔ سورج کی روشنی اور نمی سے محفوظ رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔ انجکشن کے لیک، محلول کے دھندلا ہونے یا کسی بھی قسم کی غیر حل پزیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔

A product of:

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