For the use of only a registered medical practitioner or hospital or laboratory

Biocon

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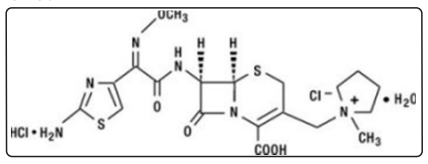
Cefepime Injection IP 1g

CELRIM® सेलरिम

COMPOSITION:
Each Vial Contains:
Cefepime HCL I.P. (Sterile)
Equivalent to Anhydrous Cefepime ..... 1000 mg
(A Sterile Mixture of Cefepime HCL and Arginine)

Pharmaceutical Form: Powder for reconstitution (IV/IM use only).
ATC Code: J01DE01

DESCRIPTION
CELRIM®(Cefepime Injection IP) contains Cefepime hydrochloride IP which is a semi-synthetic, broad spectrum, cephalosporin antibiotic for parenteral administration. The chemical name is 1-[[(6R,7R)-7-[2-(2-amino-4-thiazolyl)-glyoxylamido]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0] oct-2-en-3-yl]methyl]-1-methylpyrrolidinium chloride, 72-(Z)-(O-methyloxime), monohydrochloride, monohydrate, which corresponds to the following structural formula:



CLINICAL PHARMACOLOGY
Cefepime is an antibacterial agent belonging to the cephalosporin class of antibacterials with *in vitro* antibacterial activity against facultative Gram-positive and Gram-negative bacteria.

Pharmacokinetics
The average plasma concentrations of cefepime observed in healthy adult male volunteers (n=9) at various times following single 30-minute infusions (IV) of cefepime 500mg, 1g, and 2g are summarized in Table 1. Elimination of cefepime is principally via renal excretion with an average (±SD) half-life of 2.0 (±0.3) hours and total body clearance of 120.0 (±8.0) mL/min in healthy volunteers. Cefepime pharmacokinetics are linear over the range 250 mg to 2 g. There is no evidence of accumulation in healthy adult male volunteers (n=7) receiving clinically relevant doses for a period of 9 days.

Absorption
The average plasma concentrations of cefepime and its derived pharmacokinetic parameters after intravenous (IV) administration are portrayed in Table 1.

Table 1: Average Plasma Concentrations in mcg/mL of Cefepime and Derived Pharmacokinetic Parameters (±SD), Intravenous Administration

	CELRIM®		
Parameter	**500 mg IV**	**1 g IV**	**2 g IV**
0.5 h	38.2	78.7	163.1
1 h	21.6	44.5	85.8
2 h	11.6	24.3	44.8
4 h	5.0	10.5	19.2
8 h	1.4	2.4	3.9
12 h	0.2	0.6	1.1
C_{max}, mcg/mL	39.1 (3.5)	81.7 (5.1)	163.9 (25.3)
AUC, h•mcg/mL	70.8 (6.7)	148.5 (15.1)	284.8 (30.6)
Number of subjects (male)	9	9	9

Following intramuscular (IM) administration, cefepime is completely absorbed. The average plasma concentrations of cefepime at various times following a single intramuscular injection are summarized in Table 2. The pharmacokinetics of cefepime are linear over the range of 500 mg to 2 g intramuscularly and do not vary with respect to treatment duration.

Table 2: Average Plasma Concentrations in mcg/mL of Cefepime and Derived Pharmacokinetic Parameters (±SD), Intramuscular Administration

	CELRIM®		
Parameter	**500 mg IM**	**1 g IM**	**2 g IM**
0.5 h	8.2	14.8	36.1
1 h	12.5	25.9	49.9
2 h	12.0	26.3	51.3
4 h	6.9	16.0	31.5
8 h	1.9	4.5	8.7
12 h	0.7	1.4	2.3
C_{max}, mcg/mL	13.9 (3.4)	29.6 (4.4)	57.5 (9.5)
T_{max}, h	1.4 (0.9)	1.6 (0.4)	1.5 (0.4)
AUC, h•mcg/mL	60 (8)	137 (11)	262 (23)
Number of subjects (male)	6	6	12

Distribution
The average steady-state volume of distribution of cefepime is 18.0 (±2.0) L. The serum protein binding of cefepime is approximately 20% and is independent of its concentration in serum.
Cefepime is excreted in human milk. A nursing infant consuming approximately 1000 mL of human milk per day would receive approximately 0.5 mg of cefepime per day. Data suggest that cefepime does cross the inflamed blood-brain barrier. The clinical relevance of these data is uncertain at this time.

Metabolism and Excretion
Cefepime is metabolized to N-methylpyrrolidine (NMP) which is rapidly converted to the N-oxide (NMP-N-oxide). Urinary recovery of unchanged cefepime accounts for approximately 85% of the administered dose. Less than 1% of the administered dose is recovered from urine as NMP, 6.8% as NMP-N-oxide, and 2.5% as an epimer of cefepime. Because renal excretion is a significant pathway of elimination, patients with renal dysfunction and patients undergoing hemodialysis require dosage adjustment.

Specific Populations
Renal impairment: Cefepime pharmacokinetics have been investigated in patients with various degrees of renal impairment (n=30). The average half-life in patients requiring hemodialysis was 13.5 (±2.7) hours and in patients requiring continuous peritoneal dialysis was 19.0 (±2.0) hours. Cefepime total body clearance decreased proportionally with creatinine clearance in patients with abnormal renal function, which serves as the basis for dosage adjustment recommendations in this group of patients.

Hepatic impairment: The pharmacokinetics of cefepime were unaltered in patients with hepatic impairment who received a single 1 g dose (n=11).

Geriatric patients: Cefepime pharmacokinetics have been investigated in elderly (65 years of age and older) men (n=12) and women (n=12) whose mean (SD) creatinine clearance was 74.0 (±15.0) mL/min. There appeared to be a decrease in cefepime total body clearance as a function of creatinine clearance. Therefore, dosage administration of cefepime in the elderly should be adjusted as appropriate if the patient's creatinine clearance is 60 mL/min or less.

Microbiology
Cefepime is a bactericidal agent that acts by inhibition of bacterial cell wall synthesis. Cefepime has a broad spectrum of *in vitro* activity that encompasses a wide range of Gram-positive and Gram-negative bacteria. Cefepime has a low affinity for chromosomally-encoded beta-lactamases. Cefepime is highly resistant to hydrolysis by most beta-lactamases and exhibits rapid penetration into Gram-negative bacterial cells. Within bacterial cells, the molecular targets of cefepime are the penicillin binding proteins (PBP).

Cefepime has been shown to be active against most isolates of the following microorganisms, both *in vitro* and in clinical infections as described in the INDICATIONS AND USAGE section.

Aerobic Gram-Negative Microorganisms: *Enterobacter, Escherichia coli, Klebsiella pneumonia, Proteus mirabilis, Pseudomonas aeruginosa.*

Aerobic Gram-Positive Microorganisms: *Staphylococcus aureus, Streptococcus pneumonia, Streptococcus pyogenes , Viridans group streptococci*

The following *in vitro* data are available, but their clinical significance is unknown. Cefepime has been shown to have *in vitro* activity against most isolates of the following microorganisms; however, the safety and effectiveness of cefepime in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled trials.

Aerobic Gram-Positive Microorganisms: *Staphylococcus epidermidis* (methicillin-susceptible isolates only) *Staphylococcus saprophyticus, Streptococcus agalactiae.*
NOTE: Most isolates of enterococci, eg, Enterococcus faecalis, and methicillin-resistant staphylococci are resistant to cefepime.

Aerobic Gram-Negative Microorganisms: *Acinetobacter calcoaceticus subsp. Lwoffii, Citrobacter diversus, Citrobacter freundii, Enterobacter agglomerans, Haemophilus influenzae* (including beta-lactamase producing isolates), *Hafnia alvei, Klebsiella oxytoca, Moraxella catarrhalis (*including beta-lactamase producing isolates). *Morganella morganii, Proteus vulgaris, Providencia rettgeri, Providencia stuartii, Serratia marcescens.*
NOTE: Cefepime is inactive against many isolates of Stenotrophomonas (formerly Xanthomonas maltophilia and Pseudomonas maltophilia). Cefepime is also inactive against most isolates of Clostridium difficile.

Susceptibility Tests
Dilution Techniques
Quantitative methods are used to determine antimicrobial minimum inhibitory concentration (MIC). These MIC provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MIC should be determined using a standardized procedure. Standardized procedures are based on a dilution method or equivalent with standardized inoculum concentrations and standardized concentrations of cefepime powder. The MIC values should be interpreted according to the following criteria:

	MIC (mcg/mL)		
Microorganism	**Susceptible (S)**	**Intermediate (I)**	**Resistant (R)**
Microorganisms other than *Haemophilus* spp.* and *Streptococcus pneumoniae**	≤ 8	16	≥ 32
spp.*	≤ 2	—*	—*
	≤0.5	1	≥ 2

Haemophilus
*S. pneumoniae**

*NOTE: Isolates from these species should be tested for susceptibility using specialized dilution testing methods. Also, isolates of Haemophilus spp. with MIC greater than 2 mcg/mL should be considered equivocal and should be further evaluated.

INDICATIONS AND USAGE
CELRIM® is indicated in the treatment of the following infections caused by susceptible strains of the designated microorganisms

Pneumonia (moderate to severe) caused by *Streptococcus pneumoniae*, including cases associated with c*oncurrent bacteremia, Pseudomonas aeruginosa, Klebsiella pneumoniae, or Enterobacter* species.

Empiric Therapy for Febrile Neutropenic Patients Cefepime as monotherapy is indicated for empiric treatment of febrile neutropenic patients. In patients at high risk for severe infection (including patients with a history of recent bone marrow transplantation, with hypotension at presentation, with an underlying hematologic malignancy, or with severe or prolonged neutropenia), antimicrobial monotherapy may not be appropriate. Insufficient data exist to support the efficacy of cefepime monotherapy in such patients.

Uncomplicated and Complicated Urinary Tract Infections (including pyelonephritis) caused by *Escherichia coli or Klebsiella pneumoniae,* when the infection is severe, or caused by *Escherichia coli, Klebsiella pneumoniae, or Proteus mirabilis,* when the infection is mild to moderate, including cases associated with concurrent bacteremia with these microorganisms.

Uncomplicated Skin and Skin Structure Infections caused by *Staphylococcus aureus* (methicillin-susceptible strains only) or *Streptococcus pyogenes.*

Complicated Intra-abdominal Infections (used in combination with metronidazole) caused by *Escherichia coli, viridans* group *streptococci, Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterobacter* species, or *Bacteroides fragilis*.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of **CELRIM®** and other antibacterial drugs, **CELRIM®** should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

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

WARNINGS

BEFORE THERAPY WITH CELRIM® FOR INJECTION IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS IMMEDIATE HYPERSENSITIVITY REACTIONS TO CEFEPIME, CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. IF THIS PRODUCT IS TO BE GIVEN TO PENICILLIN-SENSITIVE PATIENTS, CAUTION SHOULD BE EXERCISED BECAUSE CROSS-HYPERSENSITIVITY AMONG BETA-LACTAM ANTIBIOTICS HAS BEEN CLEARLY DOCUMENTED AND MAY OCCUR IN UP TO 10% OF PATIENTS WITH A HISTORY OF PENICILLIN ALLERGY. IF AN ALLERGIC REACTION TO CELRIM® OCCURS, DISCONTINUE THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE TREATMENT WITH EPINEPHRINE AND OTHER EMERGENCY MEASURES INCLUDING OXYGEN, CORTICOSTEROIDS, INTRAVENOUS FLUIDS, INTRAVENOUS ANTIHISTAMINES, PRESSOR AMINES, AND AIRWAY MANAGEMENT, AS CLINICALLY INDICATED.

In patients with creatinine clearance less than or equal to 60 mL/min, the dose of **CELRIM®** (Cefepime Injection IP) should be adjusted to compensate for the slower rate of renal elimination. Because high and prolonged serum antibiotic concentrations can occur from usual dosages in patients with renal impairment or other conditions that may compromise renal function, the maintenance dosage should be reduced when cefepime is administered to such patients. Continued dosage should be determined by degree of renal impairment, severity of infection, and susceptibility of the causative organisms.

During postmarketing surveillance, serious adverse events have been reported including life-threatening or fatal occurrences of the following: encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), myoclonus, and seizures. Most cases occurred in patients with renal impairment who received doses of cefepime that exceeded the recommended dosage schedules. However, some cases of encephalopathy occurred in patients receiving a dosage adjustment for their renal function. In the majority of cases, symptoms of neurotoxicity were reversible and resolved after discontinuation of cefepime and/or after hemodialysis.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including **CELRIM®**, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile. C. difficile* produces toxins A and B, which contribute to the development of CDAD. Hypertoxin-producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

PRECAUTIONS
General
Prescribing **CELRIM®** 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.

As with other antimicrobials, prolonged use of **CELRIM®** may result in overgrowth of nonsusceptible microorganisms. Repeated evaluation of the patient's condition is essential. Should superinfection occur during therapy, appropriate measures should be taken.

Many cephalosporins, including cefepime, have been associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment, or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy. Prothrombin time should be monitored in patients at risk, and exogenous vitamin K administered as indicated.

Positive direct Coombs' tests have been reported during treatment with **CELRIM®**. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs' test may be due to the drug.

CELRIM® (Cefepime Injection IP) should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Arginine has been shown to alter glucose metabolism and elevate serum potassium transiently when administered at 33 times the amount provided by the maximum recommended human dose of **CELRIM®**. The effect of lower doses is not presently known.

Drug Interactions
Renal function should be monitored carefully if high doses of aminoglycosides are to be administered with **CELRIM®** because of the increased potential of nephrotoxicity and ototoxicity of aminoglycoside antibiotics. Nephrotoxicity has been reported

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following concomitant administration of other cephalosporins with potent diuretics such as furosemide.

Carcinogenesis, Mutagenesis, Impairment of Fertility
No animal carcinogenicity studies have been conducted with cefepime. In chromosomal aberration studies, cefepime was positive for clastogenicity in primary human lymphocytes, but negative in Chinese hamster ovary cells. In other *in vitro* assays (bacterial and mammalian cell mutation, DNA repair in primary rat hepatocytes, and sister chromatid exchange in human lymphocytes), cefepime was negative for genotoxic effects. Moreover, *in vivo* assessments of cefepime in mice (2 chromosomal aberration and 2 micronucleus studies) were negative for clastogenicity. No untoward effects on fertility were observed in rats when cefepime was administered subcutaneously at doses up to 1000 mg/kg/day (1.6 times the recommended maximum human dose calculated on a mg/m^2 basis).

Pregnancy
Teratogenic Effects: Pregnancy Category B
Cefepime was not teratogenic or embryocidal when administered during the period of organogenesis to rats at doses up to 1000 mg/kg/day (1.6 times the recommended maximum human dose calculated on a mg/m^2 basis) or to mice at doses up to 1200 mg/kg/day (approximately equal to the recommended maximum human dose calculated on a mg/m^2 basis) or to rabbits at a dose level of 100 mg/kg/day (0.3 times the recommended maximum human dose calculated on a mg/m^2 basis). There are, however, no adequate and well-controlled studies of cefepime use in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers
Cefepime is excreted in human breast milk in very low concentrations (0.5 mcg/mL). Caution should be exercised when cefepime is administered to a nursing woman.

Labor and Delivery
Cefepime has not been studied for use during labor and delivery. Treatment should only be given if clearly indicated.

Pediatric Use
The safety and effectiveness of cefepime in the treatment of uncomplicated and complicated urinary tract infections (including pyelonephritis), uncomplicated skin and skin structure infections, pneumonia, and as empiric therapy for febrile neutropenic patients have been established in the age groups 2 months up to 16 years. Use of **CELRIM®** in these age groups is supported by evidence from adequate and well-controlled studies of cefepime in adults with additional pharmacokinetic and safety data from pediatric trials.
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. This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and renal function should be monitored.

ADVERSE REACTIONS
In clinical trials using multiple doses of cefepime with the recommended dosages of cefepime (500 mg to 2 g intravenous every 12 hours),there were no deaths or permanent disabilities thought related to drug toxicity. The following adverse events were thought to be probably related to cefepime during evaluation of the drug in clinical trials..

INCIDENCE EQUAL TO OR GREATER THAN 1%	Local reactions (3.0%), including phlebitis (1.3%), pain and/or inflammation (0.6%)*; rash (1.1%)
INCIDENCE LESS THAN 1% BUT GREATER THAN 0.1%	Colitis (including pseudomembranous colitis), diarrhea, fever, headache, nausea, oral moniliasis, pruritus, urticaria, vaginitis, vomiting

* Local reactions, irrespective of relationship to cefepime in those patients who received intravenous infusion .

At the higher dose of 2 g every 8 hours, the incidence of probably-related adverse events was higher among the patients who received this dose of cefepime. They consisted of rash (4%), diarrhea (3%), nausea (2%), vomiting (1%), pruritus (1%), fever (1%), and headache (1%).

The following adverse laboratory changes, irrespective of relationship to therapy with cefepime, were seen during clinical trials.

INCIDENCE EQUAL TO OR GREATER THAN 1%	Positive Coombs' test (without hemolysis) (16.2%); decreased phosphorus (2.8%); increased ALT/SGPT (2.8%), AST/SGOT (2.4%); eosinophils (1.7%); abnormal PTT (1.6%), PT (1.4%)
INCIDENCE LESS THAN 1% BUT GREATER THAN 0.1%	Increased alkaline phosphatase, BUN, calcium, creatinine, phosphorus, potassium, total bilirubin; decreased calcium*, hematocrit, neutrophils, platelets, WBC

* Hypocalcemia was more common among elderly patients. Clinical consequences from changes in either calcium or phosphorus were not reported.

Post marketing Experience
In addition to the events reported in clinical trials with cefepime, the following adverse experiences have been reported during worldwide postmarketing experience.

As with some other drugs in this class, encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), myoclonus, and seizures have been reported. Although most cases occurred in patients with renal impairment who received doses of cefepime that exceeded the recommended dosage schedules, some cases of encephalopathy occurred in patients receiving a dosage adjustment for their renal function.

If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated. Precautions should be taken to adjust daily dosage in patients with renal insufficiency or other conditions that may compromise renal function to reduce antibiotic concentrations that can lead or contribute to these and other serious adverse events, including renal failure.

As with other cephalosporins, anaphylaxis including anaphylactic shock, transient leukopenia, neutropenia, agranulocytosis and thrombocytopenia have been reported.

Cephalosporin-Class Adverse Reactions
In addition to the adverse reactions listed above that have been observed in patients treated with cefepime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics:

Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, renal dysfunction, toxic nephropathy, aplastic anemia, hemolytic anemia, hemorrhage, hepatic dysfunction including cholestasis, and pancytopenia.

OVERDOSAGE
Patients who receive an overdose should be carefully observed and given supportive treatment. In the presence of renal insufficiency, hemodialysis, not peritoneal dialysis, is recommended to aid in the removal of cefepime from the body. Accidental overdosing has occurred when large doses were given to patients with impaired renal function. Symptoms of overdose include encephalopathy (disturbance of consciousness including confusion, hallucinations, stupor, and coma), myoclonus, seizures, and neuromuscular excitability.

DOSAGE AND ADMINISTRATION
The recommended adult and pediatric dosages and routes of administration are outlined in the following table. **CELRIM®** should be administered intravenously over approximately 30 minutes.

Site and Type of Infection	**Dose**	**Frequency**	**Duration (days)**
Adults			
Moderate to Severe Pneumonia due to *S. pneumoniae**, *P. aeruginosa*, *K. pneumoniae*, or *Enterobacter* species	1–2 g IV	Every 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, due to *E. coli, K. pneumoniae, or P. mirabilis**	0.5–1 g IV/IM***	Every 12 hours	7–10
Severe Uncomplicated or Complicated Urinary Tract Infections, including pyelonephritis, due to *E. coli* or *K. pneumoniae**	2 g IV	Every 12 hours	10
Moderate to Severe Uncomplicated Skin and Skin Structure Infections due to *S. aureus* or *S. pyogenes*	2 g IV	Every 12 hours	10
Complicated Intra-abdominal Infections (used in combination with metronidazole) caused by *E. coli*, viridans group streptococci, *P. aeruginosa* , *K. pneumoniae*, *Enterobacter* species, or *B. fragilis.*	2 g IV	Every 12 hours	7-10

*including cases associated with concurrent bacteremia
**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* when the intramuscular route is considered to be a more appropriate route of drug administration.
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 uncomplicated and complicated urinary tract infections (including pyelonephritis), uncomplicated skin and skin structure infections, and pneumonia is 50 mg per kg per dose, administered every 12 hours (50 mg per kg per dose, every 8 hours for febrile neutropenic patients), for durations as given above.

Patients with Hepatic Impairment
No adjustment is necessary for patients with hepatic impairment.

Patients with Renal Impairment
In patients with creatinine clearance less than or equal to 60 mL/min, the dose of **CELRIM®** should be adjusted to compensate for the slower rate of renal elimination. The recommended initial dose of **CELRIM®** should be the same as in patients with normal renal function except in patients undergoing hemodialysis. The recommended doses of **CELRIM®** in patients with renal impairment are presented below.

Creatinine Clearance (mL/min)	**Recommended Maintenance Schedule**			
Greater than 60 Normal recommended dosing schedule	500 mg every 12 hours	1 g every 12 hours	2 g every 12 hours	2 g every 8 hours
30–60	500 mg every 24 hours	1 g every 24 hours	2 g every 24 hours	2 g every 12 hours
11–29	500 mg every 24 hours	500 mg every 24 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 24 hours	1 g every 24 hours
CAPD	500 mg every 48 hours	1 g every 48 hours	2 g every 48 hours	2g every 48 hours
Hemodialysis*	1 g on day 1, then 500 mg every 24 hours thereafter			1 g every 24 hours

Administration
For Intravenous Infusion, constitute the 500 mg, 1g, or 2g vial, and add an appropriate quantity of the resulting solution to an intravenous container with one of the compatible intravenous fluids listed in the Compatibility and Stability subsection. THE RESULTING SOLUTION SHOULD BE ADMINISTERED OVER APPROXIMATELY 30 MINUTES.

Intramuscular Administration: For intramuscular administration, **CELRIM®** (Cefepime Injection IP) should be constituted with one of the following diluents: Sterile Water for Injection, 0.9% Sodium Chloride, 5% Dextrose Injection, 0.5% or 1.0% Lidocaine Hydrochloride, or Sterile Bacteriostatic Water for Injection with Parabens or Benzyl Alcohol.

Single-Dose Vials for Intravenous/Intramuscular Administration	**Amount of Diluent to be added (mL)**	**Approximate AvailableVolume (mL)**	**Approximate Cefepime Concentration (mg/mL)**
cefepime vial content			
500 mg (IV)	5	5.6	100
500 mg (IM)	1.3	1.8	280
1 g (IV)	10	11.3	100
1 g (IM)	2.4	3.6	280
2 g (IV)	10	12.5	160

Compatibility and Stability
Intravenous: CELRIM® is compatible at concentrations between 1 mg per mL and 40 mg per mL with the following intravenous infusion fluids: 0.9% Sodium Chloride Injection, 5% and 10% Dextrose Injection, M/6 Sodium Lactate Injection, 5% Dextrose and 0.9% Sodium Chloride Injection, Lactated Ringers and 5% Dextrose Injection. These solutions may be stored up to 24 hours at temperature 20°-25°C (68°-77°F) or 7 days in a refrigerator 2°-8°C (36°-46°F).

Solutions of **CELRIM®**, like those of most beta-lactam antibiotics, should not be added to solutions of ampicillin at a concentration greater than 40 mg per mL, and should not be added to metronidazole, vancomycin, gentamicin, tobramycin, netilmicin sulfate, or aminophylline because of potential interaction. However, if concurrent therapy with **CELRIM®** is indicated, each of these antibiotics can be administered separately.

Intramuscular: CELRIM® (Cefepime Injection IP) constituted as directed is stable for 24 hours at temperature 20°–25°C (68°–77°F) or for 7 days in a refrigerator 2°-8°C (36°–46°F) with the following diluents: Sterile Water for Injection, 0.9% Sodium Chloride Injection, 5% Dextrose Injection, Sterile Bacteriostatic Water for Injection with Parabens or Benzyl Alcohol, or 0.5% or 1% Lidocaine Hydrochloride.

NOTE: PARENTERAL DRUGS SHOULD BE INSPECTED VISUALLY FOR PARTICULATE MATTER BEFORE ADMINISTRATION.

As with other cephalosporins, the color of **CELRIM®** 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.

Storage
Store at a temperature not exceeding 30°C. Protect from light.
Keep out of reach of children.

Shelf life: Please refer to carton/label.

How Supplied
CELRIM® is available as vial of 1g

Marketed by:
Biocon Biologics India Limited
Biocon House, Semicon Park,
Electronics City, Phase - II,
Bengaluru - 560 100, India.

® - Registered trademark

Leaflet revised August 2019

To report adverse events and/or product complaints visit our website **www.biocon.com** or call toll free No: **1800 102 9465** or e-mail us at **drugsafety@biocon.com**

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