HIKMA CEFAZOLIN®

Cefazolin (as sodium)

INDICATIONS

Cefazolin is indicated in the treatment of the following infections due to susceptible organisms:

Respiratory Tract Infections

Due to S. pneumoniae, S aureus (including β-lactamase–producing strains) and S. pyogenes.

Injectable benzathine penicillin is considered to be the drug of choice in treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever.

Cefazolin is effective in the eradication of *streptococci* from the nasopharynx; however, data establishing the efficacy of Cefazolin in the subsequent prevention of rheumatic fever are not available.

Urinary Tract Infections: Due to *E. coli, P mirabilis.*

Skin and Skin Structure Infections: Due to S. aureus (including β-lactamase–producing strains), *S. pyogenes*, and other strains of *streptococci.*

Biliary Tract Infections: Due to *E. coli*, various strains of *streptococci*, *P. mirabilis*, and *S. aureus.*

Bone and Joint Infections: Due to S. aureus.

Genital Infections: (i.e., *prostatitis, epididymitis*) due to *E. coli*, *P. mirabilis.*

Septicemia: Due to *S. pneumoniae, S. aureus* (including β-lactamase–producing strains), *P. mirabilis, E. coli.*

Endocarditis: Due to *S. aureus* (including β-lactamase–producing strains) and *S. pyogenes.* Appropriate culture and susceptibility studies should be performed to determine susceptibility of the causative organism to Cefazolin.

Perioperative Prophylaxis: The prophylactic administration of Cefazolin preoperatively, intraoperatively, and postoperatively may reduce the incidence of certain postoperative infections in patients undergoing surgical procedures which are classified as contaminated or potentially contaminated (e.g., vaginal hysterectomy, and cholecystectomy in high-risk patients such as those older than 70 years, with acute cholecystitis, obstructive jaundice, or common duct bile stones).

The perioperative use of Cefazolin may also be effective in surgical patients in whom infection at the operative site would present a serious risk (e.g., during open-heart surgery and prosthetic arthroplasty).

The prophylactic administration of Cefazolin should usually be discontinued within a 24-hour period after the surgical procedure.

In surgery where the occurrence of infection may be particularly devastating (e.g., open-heart surgery and prosthetic arthroplasty), the prophylactic administration of Cefazolin may be continued for 3 to 5 days following the completion of surgery.

If there are signs of infection, specimens for cultures should be obtained for the identification of the causative organism so that appropriate therapy may be instituted.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cefazolin and other antibacterial drugs, Cefazolin 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.

DOSAGE AND ADMINISTRATION

Usual Adult Dosage

Type of Infection	Dose	Frequency
Moderate to severe infections	500 mg to 1 gram	every 6 to 8 hrs.
Mild infections caused by susceptible gram-positive cocci	250 mg to 500 mg	every 8 hours
Acute, uncomplicated urinary tract infections	1 gram	every 12 hours
Pneumococcal pneumonia	500 mg	every 12 hours
Severe, life-threatening infections (e.g., endocarditis, septicemia)*	1 gram to 1.5 grams	every 6 hours

*In rare instances, doses of up to 12 grams of Cefazolin per day have been used.

Perioperative Prophylactic Use

To prevent postoperative infection in contaminated or potentially contaminated surgery, recommended doses are:

a. 1 gram IV or IM administered 1/2 hour to 1 hour prior to the start of surgery.
b. For lengthy operative procedures (e.g., 2 hours or more), 500 mg to 1 gram IV or IM during surgery (administration modified depending on the duration of the operative procedure).
c. 500 mg to 1 gram IV or IM every 6 to 8 hours for 24 hours postoperatively.

It is important that (1) the preoperative dose be given just (1/2 to 1 hour) prior to the start of surgery so that adequate antibiotic levels are present in the serum and tissues at the time of initial surgical incision; and (2) Cefazolin be administered, if necessary, at appropriate intervals during surgery to provide sufficient levels of the antibiotic at the anticipated moments of greatest exposure to infective organisms.

In surgery where the occurrence of infection may be particularly devastating (e.g., open-heart surgery and prosthetic arthroplasty), the prophylactic administration of Cefazolin may be continued for 3 to 5 days following the completion of surgery.

Dosage Adjustment for Patients With Reduced Renal Function

Cefazolin may be used in patients with reduced renal function with the following dosage adjustments: Patients with a creatinine clearance of 55 ml/min. or greater or a serum creatinine of 1.5 mg % or less can be given full doses. Patients with creatinine clearance rates of 35 to 54 ml/min. or serum creatinine of 1.6 to 3.0 mg % can also be given full doses but dosage should be restricted to at least 8 hour intervals. Patients with creatinine clearance rates of 11 to 34 ml/min. or serum creatinine of 3.1 to 4.5 mg % should be given 1/2 the usual dose every 12 hours. Patients with creatinine clearance rates of 10 ml/min. or less or serum creatinine of 4.6 mg % or greater should be given 1/2 the usual dose every 18 to 24 hours. All reduced dosage recommendations apply after an initial loading dose appropriate to the severity of the infection. Patients undergoing peritoneal dialysis.

Pediatric Dosage

In pediatric patients, a total daily dosage of 25 to 50 mg per kg (approximately 10 to 20 mg per pound) of body weight, divided into 3 or 4 equal doses, is effective for most mild to moderately severe infections. Total daily dosage may be increased to 100 mg per kg (45 mg per pound) of body weight for severe infections. Since safety for use in premature infants and in neonates has not been established, the use of Cefazolin in these patients is not recommended.

Pediatric Dosage Guide					
Weight		25 mg/kg/day Divided into 3 Doses		25 mg/kg/day Divided into 4 Doses	
Lbs	Kg	Approximate Single Dose mg/q8h	Vol. (ml) needed with dilution of 125 mg/ml	Approximate Single Dose mg/q6h	Vol. (ml) needed with dilution of 125 mg/ml
10	4.5	40 mg	0.35 ml	30 mg	0.25 ml
20	9.0	75 mg	0.60 ml	55 mg	0.45 ml
30	13.6	115 mg	0.90 ml	85 mg	0.70 ml
40	18.1	150 mg	1.20 ml	115 mg	0.90 ml
50	22.7	190 mg	1.50 ml	140 mg	1.10 ml

Weight		50 mg/kg/day Divided into 3 Doses		50 mg/kg/day Divided into 4 Doses	
Lbs	Kg	Approximate Single Dose mg/q8h	Vol. (ml) needed with dilution of 225 mg/ml	Approximate Single Dose mg/q6h	Vol. (ml) needed with dilution of 225 mg/ml
10	4.5	75 mg	0.35 ml	55 mg	0.25 ml
20	9.0	150 mg	0.70 ml	110 mg	0.50 ml
30	13.6	225 mg	1.00 ml	170 mg	0.75 ml
40	18.1	300 mg	1.35 ml	225 mg	1.00 ml
50	22.7	375 mg	1.70 ml	285 mg	1.25 ml

In pediatric patients with mild to moderate renal impairment (creatinine clearance of 70 to 40 ml/min.), 60 percent of the normal daily dose given in equally divided doses every 12 hours should be sufficient. In patients with moderate impairment (creatinine clearance of 40 to 20 ml/min.), 25 percent of the normal daily dose given in equally divided doses every 12 hours should be adequate. Pediatric patients with severe renal impairment (creatinine clearance of 20 to 5 ml/min.) may be given 10 percent of the normal daily dose every 24 hours. All dosage recommendations apply after an initial loading dose.

Reconstitution

Preparation of Parenteral Solution

Parenteral drug products should be SHAKEN WELL when reconstituted, and inspected visually for particulate matter prior to administration. If particulate matter is evident in reconstituted fluids, the drug solutions should be discarded.

When reconstituted or diluted according to the instructions below, Cefazolin is stable for 24 hours at room temperature or for 10 days if stored under refrigeration (5°C or 41°F). Reconstituted solutions may range in color from pale yellow to yellow without a change in potency.

Single-Dose Vials

For IM injection, IV direct (bolus) injection or IV infusion, reconstitute with Sterile Water for Injection according to the following table. SHAKE WELL.

Vial Size	Amount of Diluent	Approximate-Concentration	Approximate Available Volume
1 gram	2.5 ml	330 mg/ml	3.0 ml

Pharmacy Bulk Vials

Add Sterile Water for Injection, Bacteriostatic Water for Injection, or Sodium Chloride Injection according to the table below. SHAKE WELL. Use promptly. (Discard vial within 4 hours after initial entry.)

Vial Size	Amount of Diluent	Approximate-Concentration	Approximate Available Volume
10 grams	45 ml	1 gram/5 ml	51 ml
	96 ml	1 gram/10 ml	102 ml

"Piggyback" Vials

Reconstitute with 50 to 100 ml of Sodium Chloride Injection or other

IV solution listed under ADMINISTRATION. When adding diluent to vial, allow air to escape by using a small vent needle or by pumping the syringe. SHAKE WELL. Administer with primary IV fluids, as a single dose.

Administration

Intramuscular Administration

Reconstitute vials with Sterile Water for Injection according to the dilution table above. Shake well until dissolved. Cefazolin should be injected into a large muscle mass. Pain on injection is infrequent with Cefazolin.

Intravenous Administration

Direct (bolus) injection: Following reconstitution according to the above table, further dilute vials with approximately 5 ml Sterile Water for Injection. Inject the solution slowly over 3 to 5 minutes, directly or through tubing for patients receiving parenteral fluids.

Intermittent or continuous infusion: Dilute reconstituted Cefazolin in 50 to 100 ml of 1 of the following solutions:

Sodium Chloride Injection, USP
5% or 10% Dextrose Injection, USP
5% Dextrose in Lactated Ringer's Injection, USP
5% Dextrose and 0.9% Sodium Chloride Injection, USP
5% Dextrose and 0.45% Sodium Chloride Injection, USP
5% Dextrose and 0.2% Sodium Chloride Injection, USP
Lactated Ringer's Injection, USP
Invert Sugar 5% or 10% in Sterile Water for Injection
Ringer's Injection, USP
5% Sodium Bicarbonate Injection, USP

CONTRAINDICATIONS

Cefazolin is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

WARNINGS

Before therapy with Cefazolin is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cefazolin, cephalosporins, penicillins, or other drugs. If this product is 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 Cefazolin occurs, discontinue treatment with the drug. Serious acute hypersensitivity reactions may require treatment with epinephrine and other emergency measures, including oxygen, iv fluids, iv antihistamines, corticosteroids, pressor amines, and airway management, as clinically indicated.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefazolin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by Clostridium difficile is a primary cause of "antibiotic-associated colitis".

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an oral antibacterial drug clinically effective against C. difficile colitis.

PRECAUTIONS

General

Prolonged use of Cefazolin may result in the overgrowth of nonsusceptible organisms. Careful clinical observation of the patient is essential.

When Cefazolin is administered to patients with low urinary output because of impaired renal function, lower daily dosage is required.

As with other β-lactam antibiotics, seizures may occur if inappropriately high doses are administered to patients with impaired renal function.

Cefazolin, as with all cephalosporins, should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Cephalosporins may be 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, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.

Prescribing Cefazolin 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.

Pregnancy

Teratogenic Effects

Pregnancy Category B. Reproduction studies have been performed in rats, mice, and rabbits at doses up to 25 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Cefazolin. There are, however, no adequate and well-controlled studies 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.

Labor and Delivery

When cefazolin has been administered prior to caesarean section, drug levels in cord blood have been approximately one quarter to one third of maternal drug levels. The drug appears to have no adverse effect on the fetus.

Nursing Mothers

Cefazolin is present in very low concentrations in the milk of nursing mothers. Caution should be exercised when Cefazolin is administered to a nursing woman.

Pediatric Use

Safety and effectiveness for use in premature infants and neonates have not been established.

Geriatric Use

Of the 920 subjects who received Cefazolin in clinical studies, 313 (34%) were 65 years and over, while 138 (15%) were 75 years and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

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 it may be useful to monitor renal function.

Drug Interactions

Probenecid may decrease renal tubular secretion of cephalosporins when used concurrently, resulting in increased and more prolonged cephalosporin blood levels.

SIDE EFFECTS

The following reactions have been reported:

Gastrointestinal: Diarrhea, oral candidiasis (oral thrush), vomiting, nausea, stomach cramps, anorexia, and pseudomembranous colitis. Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment. Nausea and vomiting have been reported rarely.

Allergic: Anaphylaxis, eosinophilia, itching, drug fever, skin rash, Stevens-Johnson syndrome.

Hematologic: Neutropenia, leukopenia, thrombocytopenia, thrombocythemia.

Hepatic: Transient rise in SGOT, SGPT, and alkaline phosphatase levels has been observed. As with other cephalosporins, reports of hepatitis have been received.

Renal: As with other cephalosporins, reports of increased BUN and creatinine levels, as well as renal failure, have been received.

Local Reactions: Rare instances of phlebitis have been reported at site of injection. Pain at the site of injection after intramuscular administration has occurred infrequently. Some induration has occurred.

Other Reactions: Genital and anal pruritus (including vulvar pruritus, genital moniliasis, and vaginitis).

STORAGE

Store between 15-25°C.

PRESENTATIONS

Vial:

HIKMA CEFAZOLIN 500 IV: Cefazolin (as sodium) USP 500 mg
HIKMA CEFAZOLIN 1000 IV: Cefazolin (as sodium) USP 1000 mg
HIKMA CEFAZOLIN 500 IM: Cefazolin (as sodium) USP 500 mg
HIKMA CEFAZOLIN 1000 IM: Cefazolin (as sodium) USP 1000 mg

Council of Arab Health Ministers, Union of Arab Pharmacists

THIS IS A MEDICAMENT

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous.
- Follow the doctor's prescription strictly, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

Manufactured by:
Hikma Farmaceutica Portugal
For: Hikma Pharmaceuticals, Amman – Jordan

Keep medicament out of the reach of children

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