Prescribing Information

Ceporacin®

Cephalothin Sodium BP for Injection

1 g/vial

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Date of Preparation:
March 31, 2014

Submission Control No: 172067

[Pr]Ceporacin® I.V./I.M

Cephalothin Sodium BP for Injection

THERAPEUTIC CATEGORY: ANTIBIOTIC

ACTION:

Ceporacin® (cephalothin sodium) is a bacterial antibiotic. It kills susceptible bacterial cells by inhibiting cell wall synthesis.

INDICATIONS:

May be indicated for the treatment of serious infections caused by susceptible strains of the designated microorganisms in the diseases listed below. Culture and susceptibility studies should be performed. Clinical judgement and anticipated bacteriological findings may permit the start of therapy before results of susceptibility studies are obtained. Respiratory tract infections caused by *S. pneumonia, staphylococcus spp.* (beta-lactamase and nonbeta-lactamase (penicillinase) producing). Group A beta-hemolytic *streptococcus spp.*, *Klebsiella spp.*, and *H.influenzae.*

Skin and soft tissue infections, including peritonitis caused by *staphylococcus spp.* (beta-lactamase and nonbeta-lactamase producing). Group A beta-hemolytic *streptococcus spp.*, *E. coli, P.mirabilis*, and *Klebsiella spp.*

Genitourinary tract infections caused by *E. coli, P.mirabilis*, and *Klebsiella spp.*

Septicemia, including endocarditis, caused by *S.pneumoniae, staphylococcus spp.* (beta-lactamase and nonbeta-lactamase producing). Group A beta-hemolytic *streptococcus spp.*, *S.viridans, E. coli, P.mirabilis*, and *Klebsiella spp.*

Meningitis cause by *S.pneumoniae,* Group A beta-hemolytic *streptococcus spp.* and *staphylococcus spp.* (beta-lactamase and nonbeta-lactamase producing).

Bone and joint infections caused by *staphylococcus spp.* (beta-lactamase and nonbeta-lactamase producing).

Evidence indicates that perioperative administration of cephalothin sodium may help to reduce the incidence of postoperative infections in patients undergoing surgical procedures involving contaminated or potentially contaminated sites. It may also be effective in patients at risk of serious infection when undergoing “clean” bone and open heart surgery, gynecological, obstetric, urologic, head and neck and other types of surgery. Cephalothin sodium is not at present recommended in surgery related to the lower gastrointestinal tract or certain other sites where anaerobic organisms such as bacteroides tend to prevail. Past experience has generally involved one or two day post-operative administration of cephalothin sodium followed by oral antibiotics. Longer courses of therapy may be desirable when prosthetic devices are surgically implanted.

NOTE: If the susceptibility tests show that the causative organism is resistant to cephalothin sodium, institute other appropriate antibiotic therapy.

CONTRAINDICATIONS:

Cephalothin sodium is contraindicated in persons hypersensitive to the cephalosporins.

WARNINGS:

Before cephalothin therapy is instituted, careful inquiry should be made concerning previous hypersensitivity reactions to cephalosporins and penicillin. Cephalosporin C derivatives should be given cautiously to penicillin-sensitive patients. Serious acute hypersensivity reactions may require epinephrine and other emergency measures. There is some clinical and laboratory evidence of partial cross-allergenicity of the penicillins and cephalosporins. Patients have been reported to have had severe reactions including anaphylaxis to both drugs. Any patient who has demonstrated some form of allergy, particularly to drugs, should receive antibiotics cautiously and then only when absolutely necessary. No exception should be made with regard to cephalothin sodium.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics (including macrolides, semi-synthetic penicillins and cephalosporins); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with the use of antibiotics. Such colitis may range in severity from mild to life-threatening.

Treatment with broad spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of Clostridial spp. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Mild cases of Pseudomembranous colitis usually respond to drug discontinuance alone. In moderate to severe cases, management should include sigmoidoscopy, appropriate bacteriologic studies, and fluid, electrolyte, and protein supplementation. When the colitis does not improve after the drug has been discontinued, or when it is severe, oral vancomycin is the drug of choice for antibiotic-associated pseudomembranous colitis produced by *Cl. difficile.* Other causes of colitis should be ruled out.

PRECAUTIONS:

Patients should be followed carefully so that any side effects or unusual manifestation of drug idiosyncrasy may be detected. If an allergic reaction to cephalothin sodium occurs, the drug should be discontinued and the patient treated with the usual agents (e.g. epinephrine or other pressor amines, antihistamines, or corticosteroids).

Although cephalothin sodium rarely produces alteration in kidney functions, evaluation of renal status is recommended, especially in seriously ill patients receiving maximum doses. Patients with impaired renal function should be placed on the dosage schedule recommended under dosage and administration. Usual doses in such individuals may result in excessive serum concentrations.

Where potentially nephrotoxic agents such as potent diuretics or aminoglycoside antibiotics are administered prior to or in conjunction with cephalosporins, the risk of nephrotoxicity may be increased and renal function should be monitored.

When I.V. doses of cephalothin sodium larger than 6 g daily are given by infusion for periods longer than 3 days, they may be associated with thrombophlebitis, and the veins may have to be alternated. The use of small I.V. needles in the larger available veins may be preferred.

Prolonged use of cephalothin sodium may result in the overgrowth of nonsusceptible organisms. Constant observation of the patient is essential. If superinfection occurs during therapy, take appropriate measures.

Pregnancy: Safety of this product for use during pregnancy has not been established.

A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution or with Clinitest tablets, but not with Tes-Tape.

ADVERSE REACTIONS:

Hypersensivity – Maculopapular rash, urticarial, reactions resembling serum sickness, and anaphylaxis have been reported. Eosinophilia and drug fever have been observed to be associated with other allergic reactions, these reactions are most likely to occur in patients with a history of allergy, particularly to penicillin.

Blood – Neutropenia, thrombocytopenia, and hemolytic anemia have been reported. Some individuals, particularly those with azotemia, have developed positive direct Coombs' tests during Cephalothin sodium therapy.

Liver – Transient rise in SGOT and alkaline phosphatase has been noted.

Kidney – Rise in BUN and decreased creatinine clearance have been reported, particularly in patients with prior renal impairment. The role of cephalothin sodium in renal changes is difficult to assess because other factors predisposing to prerenal azotemia or to acute renal failure usually have been present.

Local Reactions – Pain, induration, tenderness and elevation of temperature have been reported following repeated intramuscular injections. Thrombophlebitis has occurred and is usually associated with daily doses of more than 6 g given by infusion for longer than three days.

Gastrointestinal – Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment. Nausea and vomiting have been reported rarely.

SYMPTOMS AND TREATMENT OF OVERDOSAGE:

Daily doses up to 12 g have been used successfully without evidence of untoward systemic effects. The administration of inappropriately large doses of parenteral cephalosporins may cause seizures, particularly in patients with renal impairment. Dosage reduction is necessary when renal function is impaired. If seizures occur, the drug should be promptly discontinued; anticonvulsant therapy may be administered if clinically indicated. Hemodialysis may be considered in cases of overwhelming overdosage.

As is the case with all new drugs, patients should be followed carefully so that any side-effects or unusual manifestations of drug idiosyncrasy may be detected. If an allergic reaction to

cephalothin sodium occurs, the drug should be discontinued and the patient treated with the usual agents (e.g. epinephrine, antihistamines, pressor amines, or corticosteroids).

DOSAGE: Ceporacin has been shown to be physically compatible with most commonly used I.V. fluids and electrolyte solution In general, it is not compatible with compounds of high molecular weight or with alkaline earth metals. Its addition to solutions having a pH below 4 or above 8.5 is not advised. The usual adult dosage range is 500 mg to 2 g of cephalothin every 4 to 6 hours. A dosage of 500 mg every 6 hours is adequate in uncomplicated pneumonia, furunculosis with cellulitis, and most urinary tract infections. In severe infections, this may be increased by giving the injections every 4 hours or, when the desired response is not obtained, by raising the dose to 1 g. In life-threatening infections, doses up to 2 g every 4 hours may be required. To reduce the incidence of postoperative infection in contaminated or potentially contaminated surgery, 2 g administered I.V. just prior to surgery, 2 g during surgery (is the procedure is prolonged) and 2 g every 6 hours for 1 or 2 days postoperatively is recommended. Continuation with oral antibiotics may be considered. Longer periods of cephalothin administration may also be desirable in selected surgical procedures. When renal function is reduced, an I.V. loading dose of 1 to 2 g may be given. Continued dosage schedule should be determined by degree of renal impairment, severity of infection, and sensitivity of the causative organism. The maximum doses administered should be based on the following recomandations (see Table 1)

Table 1 – Ceporacin

Maximum Doses	
Renal Function Status	**Maximum Adult Dosage (Maintenance)**
Mild Impairment (C_{cr} =80-50 mL/min)	2 g q6h
Moderate Impairment (C_{cr} =50-25 mL/min)	1.5 g q6h
Severe Impairment (C_{cr} =25-10 mL/min)	1 g q6h
Marked Impairment (C_{cr} =10-2 mL/min)	0.5 g q6h
Essentially No Function (C_{cr} = ≤ 2 mL/min)	0.5 g q8h

In infants and children, the dosage should be proportionately less in accordance with age, weight, and severity of infection. Daily administration of 100 mg/kg (80 to 160 mg/kg) in divided doses has been found effective for most infections susceptible to cephalothin. Antibiotic therapy in B-hemolytic streptococcal infections should continue for at least 10 days. In staphylococcal infections, surgical procedures, such as incision and drainage, should be carried out in all cases when indicated.

ADMINISTRATION: I.M. Cephalothin should be given by deep i.m. injection into a large muscle mass, such as the gluteus or lateral aspect of the thigh, to minimize pain and induration and the possible formation of s.c. sterile abscess.

I.V.: The i.v. route may be preferable for patients with bacteremia, septicemia, or other severe or life-threatening infections who may be poor risks because of lowered resistance resulting from such debilitating conditions as malnutrition, trauma, surgery, diabetes, heart failure, or malignancy, particularly is shock is present or impending. For these infections in patients with normal renal function, the i.v. dosage is 4 to 12 g of cephalothin daily. In conditions such as septicemia, 6 to 8 g/day may be given i.v. for several days at the beginning of therapy; then, depending on the clinical response and laboratory findings, the dosage may gradually be reduced.

Intermittent I.V.: Administration: For intermittent i.v. administration, a solution containing 1 g cephalothin in 10 mL of diluent may be slowly injected directly into the vein over a period of 3 to 5 minutes or may be given through the tubing when the patient is receiving parenteral solutions.

Intermittent i.v. infusion with a Y-type administration set can also be accomplished while bulk i.v. solutions are being infused. However, during infusion of the solution containing cephalothin, it is desirable to discontinue the other solution. When this technique is employed, careful attention should be paid to the volume of the solution containing cephalothin so that the calculated dose will be infused. See Reconstitution for specific package information.

Continuous I.V. Infusion: For continuous i.v. infusion, 2 or 4 g of cephalothin, diluted and well mixed with Sterile Water for Injection, may be added to an i.v. bottle containing 5% dextrose, normal saline solution, Lactated Ringer's injection, USP, Dextrose 5% in Lactated Ringer's Injection or 5% dextrose with 0.02% sodium bicarbonate. The choice of solution and the volume to be employed are dictated by fluid and electrolyte management.

Intraperitoneal: In peritoneal dialysis procedures, cephalothin has been added to dialysis fluid in concentrations up to 6 mg/100 mL and instilled into the peritoneal space throughout an entire dialysis (16 to 30 hours). Careful assay procedures have shown that 44% of the administered drug was absorbed into the bloodstream. Serum levels of 10ug/mL were reported, with no evidence of accumulation, and no untoward local or systemic reactions.

The intraperitoneal administration of solutions containing 0.1 to 4% cephalothin in saline has been used in threatening patients with peritonitis or contaminated peritoneal cavities. (The total

daily dosage of cephalothin should take into account the amount given by the intraperitonal route.)

Reconstitution: I.M. Reconstitute with Sterile Water for Injection. See table II.

Table II – Ceporacin

Reconstitution for I.M. use			
Vial Size	**Volume to be Added**	**Approximate Available Volume**	**Approximate Average Concentration**
1 g	4.5 mL	5 mL	200 mg/mL

Shake well until dissolved.

I.V.: Solution for Reconstitution: Sterile Water for Injection, 5% Dextrose Injection, 0.9% Sodium Chloride Injection. See table III.

Table III – Ceporacin

Reconstitution for I.V. use			
Vial Size	**Volume to be Added**	**Approximate Available Volume**	**Approximate Average Concentration**
1 g	10 mL	10.5 mL	95 mg/mL

Shake ell until dissolved. The prepared solution may be further diluted to the desired volume with any of the solutions for i.v. infusion listed below.

Solutions for I.V. Infusion: 0.9% Sodium Chloride Injection, 5% Dextrose Injection, 5% Dextrose and 0.9% Sodium Chloride Injection, 5% Dextrose and 0.45% Sodium Chloride Injection, 5% Dextrose and 0.2% Sodium Chloride Injection, 5% dextrose and 0.15 Potassium Chloride Injection, 5% Osmitrol in Water for Injection, Sodium Lactate Injection(M/6), Normosol-M in D5-W, Ionosol-B in 5% Dextrose Injection, Ringer's Injection, Acetated Ringers Injection, Lactated Ringers in 5% Dextrose Injection.

Stability: Reconstituted Ceporacin should be used within 24 hours when stored at room temperature or within 72 hours when refrigerated. Ceporacin solutions reconstituted with bacteriostatic diluent and used for i.m. administration as multiple-dose containers should be used within 7 days when stored under refrigeration.

A concentrated solution of Ceporacin may take on pale straw color when freshly mixed. This will darken upon standing at room temperature. Dark brown solutions should not be used. I.V. infusion should be completed within 24 hours after preparing the solution. For prolonged infusions, replace with a freshly prepared solution at least every 24 hours.

SUPPLIED: Vials: 1g: Each vial of sterile powder contains: cephalothin 1 g as cephalothin sodium and sodium bicarbonate 30 mg as buffer.