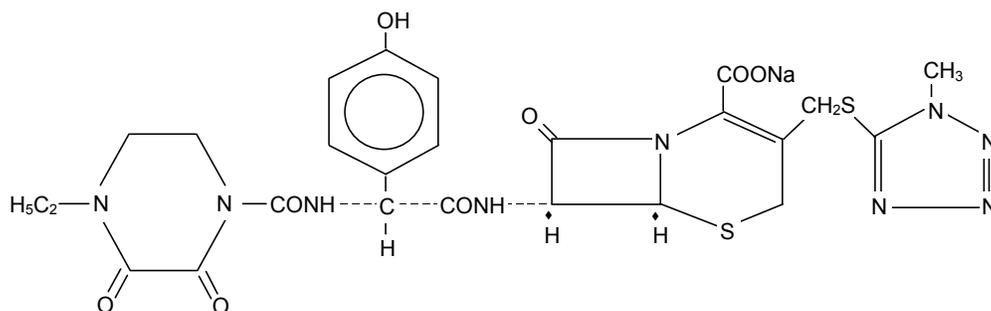


CEFOBID®
(sterile cefoperazone, USP)
Formerly known as sterile cefoperazone sodium, USP

**PHARMACY BULK PACKAGE
NOT FOR DIRECT INFUSION**

DESCRIPTION

CEFOBID® (cefoperazone), formerly known as cefoperazone sodium, is a sterile, semisynthetic, broad-spectrum, parenteral cephalosporin antibiotic for intravenous or intramuscular administration. It is the sodium salt of 7-[(*R*)-2-(4-ethyl-2,3-dioxo-1-piperazinecarboxamido)-2-(*p*-hydroxyphenyl)acetamido-3-[[1-(1-methyl-*H*-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate. Its chemical formula is $C_{25}H_{26}N_9NaO_8S_2$ with a molecular weight of 667.65. The structural formula is given below:



CEFOBID contains 34 mg sodium (1.5 mEq) per gram. CEFOBID is a white powder which is freely soluble in water. The pH of a 25% (w/v) freshly reconstituted solution varies between 4.5–6.5 and the solution ranges from colorless to straw yellow depending on the concentration.

CEFOBID in crystalline form is supplied in vials equivalent to 1 g or 2 g of cefoperazone.

A pharmacy bulk package is a container of a sterile preparation for parenteral use that contains many single doses.

This Pharmacy Bulk Package is for use in a pharmacy admixture service; it provides many single doses of cefoperazone for addition to suitable parenteral fluids in the preparation of admixtures for intravenous infusion. (See DOSAGE AND ADMINISTRATION, and DIRECTIONS FOR PROPER USE OF PHARMACY BULK PACKAGE.)

CLINICAL PHARMACOLOGY

High serum and bile levels of CEFOBID are attained after a single dose of the drug. Table 1 demonstrates the serum concentrations of CEFOBID in normal volunteers following either a single 15-minute constant rate intravenous infusion of 1, 2, 3 or 4 grams of the drug, or a single intramuscular injection of 1 or 2 grams of the drug.

TABLE 1. Cefoperazone Serum Concentrations

Dose/Route	Mean Serum Concentrations (mcg/mL)						
	0*	0.5 hr	1 hr	2 hr	4 hr	8 hr	12 hr
1 g IV	153	114	73	38	16	4	0.5
2 g IV	252	153	114	70	32	8	2
3 g IV	340	210	142	89	41	9	2
4 g IV	506	325	251	161	71	19	6
1 g IM	32**	52	65	57	33	7	1
2 g IM	40**	69	93	97	58	14	4

* Hours post-administration, with 0 time being the end of the infusion.
 ** Values obtained 15 minutes post-injection.

The mean serum half-life of CEFOBID is approximately 2.0 hours, independent of the route of administration.

In vitro studies with human serum indicate that the degree of CEFOBID reversible protein binding varies with the serum concentration from 93% at 25 mcg/mL of CEFOBID to 90% at 250 mcg/mL and 82% at 500 mcg/mL.

CEFOBID achieves therapeutic concentrations in the following body tissues and fluids:

Tissue or Fluid	Dose	Concentration
Ascitic Fluid	2 g	64 mcg/mL
Cerebrospinal Fluid (in patients with inflamed meninges)	50 mg/kg	1.8 mcg/mL to 8.0 mcg/mL
Urine	2 g	3,286 mcg/mL
Sputum	3 g	6.0 mcg/mL
Endometrium	2 g	74 mcg/g
Myometrium	2 g	54 mcg/g
Palatine Tonsil	1 g	8 mcg/g
Sinus Mucous Membrane	1 g	8 mcg/g
Umbilical Cord Blood	1 g	25 mcg/mL
Amniotic Fluid	1 g	4.8 mcg/mL
Lung	1 g	28 mcg/g
Bone	2 g	40 mcg/g

CEFOBID is excreted mainly in the bile. Maximum bile concentrations are generally obtained between one and three hours following drug administration and exceed concurrent serum concentrations by up to 100 times. Reported biliary concentrations of CEFOBID range from

66 mcg/mL at 30 minutes to as high as 6000 mcg/mL at 3 hours after an intravenous bolus injection of 2 grams.

Following a single intramuscular or intravenous dose, the urinary recovery of CEFOBID over a 12-hour period averages 20–30%. No significant quantity of metabolites has been found in the urine. Urinary concentrations greater than 2200 mcg/mL have been obtained following a 15-minute infusion of a 2 g dose. After an IM injection of 2 g, peak urine concentrations of almost 1000 mcg/mL have been obtained, and therapeutic levels are maintained for 12 hours.

Repeated administration of CEFOBID at 12-hour intervals does not result in accumulation of the drug in normal subjects. Peak serum concentrations, areas under the curve (AUC's), and serum half-lives in patients with severe renal insufficiency are not significantly different from those in normal volunteers. In patients with hepatic dysfunction, the serum half-life is prolonged and urinary excretion is increased. In patients with combined renal and hepatic insufficiencies, CEFOBID may accumulate in the serum.

CEFEBID has been used in pediatrics, but the safety and effectiveness in children have not been established. The half-life of CEFEBID in serum is 6–10 hours in low birth-weight neonates.

Microbiology

CEFEBID is active *in vitro* against a wide range of aerobic and anaerobic, gram-positive and gram-negative pathogens. The bactericidal action of CEFEBID results from the inhibition of bacterial cell wall synthesis. CEFEBID has a high degree of stability in the presence of beta-lactamases produced by most gram-negative pathogens. CEFEBID is usually active against organisms which are resistant to other beta-lactam antibiotics because of beta-lactamase production. CEFEBID is usually active against the following organisms *in vitro* and in clinical infections:

Gram-Positive Aerobes:

- *Staphylococcus aureus*, penicillinase and non-penicillinase producing strains
- *Staphylococcus epidermidis*
- *Streptococcus pneumoniae* (formerly *Diplococcus pneumoniae*)
- *Streptococcus pyogenes* (Group A beta-hemolytic streptococci)
- *Streptococcus agalactiae* (Group B beta-hemolytic streptococci)
- Enterococcus (*Streptococcus faecalis*, *S. faecium* and *S. durans*)

Gram-Negative Aerobes:

- *Escherichia coli*
- *Klebsiella* species (including *K. pneumoniae*)
- *Enterobacter* species
- *Citrobacter* species
- *Haemophilus influenzae*
- *Proteus mirabilis*
- *Proteus vulgaris*
- *Morganella morganii* (formerly *Proteus morganii*)
- *Providencia stuartii*
- *Providencia rettgeri* (formerly *Proteus rettgeri*)
- *Serratia marcescens*
- *Pseudomonas aeruginosa*
- *Pseudomonas* species
- Some strains of *Acinetobacter calcoaceticus*
- *Neisseria gonorrhoeae*

Anaerobic Organisms:

- Gram-positive cocci (including *Peptococcus* and *Peptostreptococcus*)
- *Clostridium* species
- *Bacteroides fragilis*
- Other *Bacteroides* species

CEFOBID is also active *in vitro* against a wide variety of other pathogens although the clinical significance is unknown. These organisms include: *Salmonella* and *Shigella* species, *Serratia liquefaciens*, *N. meningitidis*, *Bordetella pertussis*, *Yersinia enterocolitica*, *Clostridium difficile*, *Fusobacterium* species, *Eubacterium* species and beta-lactamase producing strains of *H. influenzae* and *N. gonorrhoeae*.

SUSCEPTIBILITY TESTING

Diffusion Technique. For the disk diffusion method of susceptibility testing, a 75 mcg CEFOBID diffusion disk should be used. Organisms should be tested with the CEFOBID 75 mcg disk since CEFOBID has been shown *in vitro* to be active against organisms which are found to be resistant to other beta-lactam antibiotics.

Tests should be interpreted by the following criteria:

Zone Diameter	Interpretation
Greater than or equal to 21 mm	Susceptible
16–20 mm	Moderately Susceptible
Less than or equal to 15 mm	Resistant

Quantitative procedures that require measurement of zone diameters give the most precise estimate of susceptibility. One such method which has been recommended for use with the CEFOBID 75 mcg disk is the NCCLS approved standard. (Performance Standards for

Antimicrobial Disk Susceptibility Tests. Second Information Supplement Vol. 2 No. 2 pp. 49–69. Publisher–National Committee for Clinical Laboratory Standards, Villanova, Pennsylvania.)

A report of “susceptible” indicates that the infecting organism is likely to respond to CEFOBID therapy and a report of “resistant” indicates that the infecting organism is not likely to respond to therapy. A “moderately susceptible” report suggests that the infecting organism will be susceptible to CEFOBID if a higher than usual dosage is used or if the infection is confined to tissues and fluids (e.g., urine or bile) in which high antibiotic levels are attained.

Dilution Techniques. Broth or agar dilution methods may be used to determine the minimal inhibitory concentration (MIC) of CEFOBID. Serial twofold dilutions of CEFOBID should be prepared in either broth or agar. Broth should be inoculated to contain 5×10^5 organisms/mL and agar “spotted” with 10^4 organisms.

MIC test results should be interpreted in light of serum, tissue, and body fluid concentrations of CEFOBID. Organisms inhibited by CEFOBID at 16 mcg/mL or less are considered susceptible, while organisms with MIC’s of 17–63 mcg/mL are moderately susceptible. Organisms inhibited at CEFOBID concentrations of greater than or equal to 64 mcg/mL are considered resistant, although clinical cures have been obtained in some patients infected by such organisms.

INDICATIONS AND USAGE

CEFEBID is indicated for the treatment of the following infections when caused by susceptible organisms:

Respiratory Tract Infections caused by *S. pneumoniae*, *H. influenzae*, *S. aureus* (penicillinase and non-penicillinase producing strains), *S. pyogenes** (Group A beta-hemolytic streptococci), *P. aeruginosa*, *Klebsiella pneumoniae*, *E. coli*, *Proteus mirabilis*, and *Enterobacter* species.

Peritonitis and Other Intra-abdominal Infections caused by *E. coli*, *P. aeruginosa*,* and anaerobic gram-negative bacilli (including *Bacteroides fragilis*).

Bacterial Septicemia caused by *S. pneumoniae*, *S. agalactiae*,* *S. aureus*, *Pseudomonas aeruginosa*,* *E. coli*, *Klebsiella* spp.,* *Klebsiella pneumoniae*,* *Proteus* species* (indole-positive and indole-negative), *Clostridium* spp.* and anaerobic gram-positive cocci.*

Infections of the Skin and Skin Structures caused by *S. aureus* (penicillinase and non-penicillinase producing strains), *S. pyogenes*,* and *P. aeruginosa*.

Pelvic Inflammatory Disease, Endometritis, and Other Infections of the Female Genital Tract caused by *N. gonorrhoeae*, *S. epidermidis*,* *S. agalactiae*, *E. coli*, *Clostridium* spp.,* *Bacteroides* species (including *Bacteroides fragilis*), and anaerobic gram-positive cocci.

Cefobid®, like other cephalosporins, has no activity against *Chlamydia trachomatis*. Therefore, when cephalosporins are used in the treatment of patients with pelvic inflammatory disease and

C. trachomatis is one of the suspected pathogens, appropriate anti-chlamydial coverage should be added.

Urinary Tract Infections caused by *Escherichia coli* and *Pseudomonas aeruginosa*.

Enterococcal Infections: Although cefoperazone has been shown to be clinically effective in the treatment of infections caused by enterococci in cases of **peritonitis and other intra-abdominal infections, infections of the skin and skin structures, pelvic inflammatory disease, endometritis and other infections of the female genital tract, and urinary tract infections,*** the majority of clinical isolates of enterococci tested are not susceptible to cefoperazone but fall just at or in the intermediate zone of susceptibility, and are moderately resistant to cefoperazone. However, *in vitro* susceptibility testing may not correlate directly with *in vivo* results. Despite this, cefoperazone therapy has resulted in clinical cures of enterococcal infections, chiefly in polymicrobial infections. Cefoperazone should be used in enterococcal infections with care and at doses that achieve satisfactory serum levels of cefoperazone.

* Efficacy of this organism in this organ system was studied in fewer than 10 infections.

Susceptibility Testing

Before instituting treatment with CEFOBID, appropriate specimens should be obtained for isolation of the causative organism and for determination of its susceptibility to the drug. Treatment may be started before results of susceptibility testing are available.

Combination Therapy

Synergy between CEFOBID and aminoglycosides has been demonstrated with many gram-negative bacilli. However, such enhanced activity of these combinations is not predictable. If such therapy is considered, *in vitro* susceptibility tests should be performed to determine the activity of the drugs in combination, and renal function should be monitored carefully. (See PRECAUTIONS, and DOSAGE AND ADMINISTRATION sections.)

CONTRAINDICATIONS

CEFOBID is contraindicated in patients with known allergy to the cephalosporin-class of antibiotics.

WARNINGS

BEFORE THERAPY WITH CEFOBID IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS, PENICILLINS OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY

REQUIRE THE USE OF SUBCUTANEOUS EPINEPHRINE AND OTHER EMERGENCY MEASURES.

PSEUDOMEMBRANOUS COLITIS HAS BEEN REPORTED WITH THE USE OF CEPHALOSPORINS (AND OTHER BROAD-SPECTRUM ANTIBIOTICS); THEREFORE, IT IS IMPORTANT TO CONSIDER ITS DIAGNOSIS IN PATIENTS WHO DEVELOP DIARRHEA IN ASSOCIATION WITH ANTIBIOTIC USE.

Treatment with broad-spectrum antibiotics alters normal flora of the colon and may permit overgrowth of clostridia. Studies indicate a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Cholestyramine and colestipol resins have been shown to bind the toxin *in vitro*.

Mild cases of colitis may respond to drug discontinuance alone.

Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated.

When the colitis is not relieved by drug discontinuance or when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile*. Other causes of colitis should also be considered.

PRECAUTIONS

Although transient elevations of the BUN and serum creatinine have been observed, CEFOBID alone does not appear to cause significant nephrotoxicity. However, concomitant administration of aminoglycosides and other cephalosporins has caused nephrotoxicity.

CEFEBID is extensively excreted in bile. The serum half-life of CEFEBID is increased 2–4 fold in patients with hepatic disease and/or biliary obstruction. In general, total daily dosage above 4 g should not be necessary in such patients. If higher dosages are used, serum concentrations should be monitored.

Because renal excretion is not the main route of elimination of CEFEBID (see CLINICAL PHARMACOLOGY), patients with renal failure require no adjustment in dosage when usual doses are administered. When high doses of CEFEBID are used, concentrations of drug in the serum should be monitored periodically. If evidence of accumulation exists, dosage should be decreased accordingly.

The half-life of CEFEBID is reduced slightly during hemodialysis. Thus, dosing should be scheduled to follow a dialysis period. In patients with both hepatic dysfunction and significant renal disease, CEFEBID dosage should not exceed 1–2 g daily without close monitoring of serum concentrations.

As with other antibiotics, vitamin K deficiency has occurred rarely in patients treated with CEFOBID. The mechanism is most probably related to the suppression of gut flora which normally synthesize this vitamin. Those at risk include patients with a poor nutritional status, malabsorption states (e.g., cystic fibrosis), alcoholism, and patients on prolonged hyper-alimentation regimens (administered either intravenously or via a naso-gastric tube). Prothrombin time should be monitored in these patients and exogenous vitamin K administered as indicated.

A disulfiram-like reaction characterized by flushing, sweating, headache, and tachycardia has been reported when alcohol (beer, wine) was ingested within 72 hours after CEFOBID administration. Patients should be cautioned about the ingestion of alcoholic beverages following the administration of CEFOBID. A similar reaction has been reported with other cephalosporins.

Prolonged use of CEFOBID may result in the overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

CEFEBID should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Drug/Laboratory Test Interactions

A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been performed to evaluate carcinogenic potential. The maximum duration of CEFEBID animal toxicity studies is six months. In none of the *in vivo* or *in vitro* genetic toxicology studies did CEFEBID show any mutagenic potential at either the chromosomal or subchromosomal level. CEFEBID produced no impairment of fertility and had no effects on general reproductive performance or fetal development when administered subcutaneously at daily doses up to 500 to 1000 mg/kg prior to and during mating, and to pregnant female rats during gestation. These doses are 10 to 20 times the estimated usual single clinical dose. CEFEBID had adverse effects on the testes of prepubertal rats at all doses tested. Subcutaneous administration of 1000 mg/kg per day (approximately 16 times the average adult human dose) resulted in reduced testicular weight, arrested spermatogenesis, reduced germinal cell population and vacuolation of Sertoli cell cytoplasm. The severity of lesions was dose dependent in the 100 to 1000 mg/kg per day range; the low dose caused a minor decrease in spermatocytes. This effect has not been observed in adult rats. Histologically the lesions were reversible at all but the highest dosage levels. However, these studies did not evaluate subsequent development of reproductive function in the rats. The relationship of these findings to humans is unknown.

Usage in Pregnancy

Pregnancy Category B: Reproduction studies have been performed in mice, rats and monkeys at doses up to 10 times the human dose and have revealed no evidence of impaired fertility or harm

to the fetus due to CEFOBID. 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.

Usage in Nursing Mothers

Only low concentrations of CEFOBID are excreted in human milk. Although CEFOBID passes poorly into breast milk of nursing mothers, caution should be exercised when CEFOBID is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in children have not been established. For information concerning testicular changes in prepubertal rats, see Carcinogenesis, Mutagenesis, Impairment of Fertility.

Geriatric Use

Clinical studies of CEFOBID[®] (sterile cefoperazone sodium) did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS

In clinical studies the following adverse effects were observed and were considered to be related to CEFOBID therapy or of uncertain etiology:

Hypersensitivity: As with all cephalosporins, hypersensitivity manifested by skin reactions (1 patient in 45), drug fever (1 in 260), or a change in Coombs' test (1 in 60) has been reported. These reactions are more likely to occur in patients with a history of allergies, particularly to penicillin.

Hematology: As with other beta-lactam antibiotics, reversible neutropenia may occur with prolonged administration. Slight decreases in neutrophil count (1 patient in 50) have been reported. Decreased hemoglobins (1 in 20) or hematocrits (1 in 20) have been reported, which is consistent with published literature on other cephalosporins. Transient eosinophilia has occurred in 1 patient in 10.

Hepatic: Of 1285 patients treated with cefoperazone in clinical trials, one patient with a history of liver disease developed significantly elevated liver function enzymes during CEFOBID therapy. Clinical signs and symptoms of nonspecific hepatitis accompanied these increases. After CEFOBID therapy was discontinued, the patient's enzymes returned to pre-treatment levels and the symptomatology resolved. As with other antibiotics that achieve high bile levels, mild transient elevations of liver function enzymes have been observed in 5–10% of the patients receiving CEFOBID therapy. The relevance of these findings, which were not accompanied by overt signs or symptoms of hepatic dysfunction, has not been established.

Gastrointestinal: Diarrhea or loose stools has been reported in 1 in 30 patients. Most of these experiences have been mild or moderate in severity and self-limiting in nature. In all cases, these symptoms responded to symptomatic therapy or ceased when cefoperazone therapy was stopped. Nausea and vomiting have been reported rarely.

Symptoms of pseudomembranous colitis can appear during or for several weeks subsequent to antibiotic therapy (see WARNINGS).

Renal Function Tests: Transient elevations of the BUN (1 in 16) and serum creatinine (1 in 48) have been noted.

Local Reactions: CEFOBID is well tolerated following intramuscular administration. Occasionally, transient pain (1 in 140) may follow administration by this route. When CEFOBID is administered by intravenous infusion some patients may develop phlebitis (1 in 120) at the infusion site.

DOSAGE AND ADMINISTRATION

Sterile cefoperazone sodium can be administered by IM or IV injection (following dilution). However, the intent of this pharmacy bulk package is for the preparation of solutions for IV infusion only.

The usual adult daily dose of CEFOBID is 2 to 4 grams per day administered in equally divided doses every 12 hours.

In severe infections or infections caused by less sensitive organisms, the total daily dose and/or frequency may be increased. Patients have been successfully treated with a total daily dosage of 6–12 grams divided into 2, 3, or 4 administrations ranging from 1.5 to 4 grams per dose.

When treating infections caused by *Streptococcus pyogenes*, therapy should be continued for at least 10 days.

If *C. trachomatis* is a suspected pathogen, appropriate anti-chlamydial coverage should be added, because cefoperazone has no activity against this organism.

Solutions of CEFOBID and aminoglycoside should not be directly mixed, since there is a physical incompatibility between them. If combination therapy with CEFOBID and an aminoglycoside is contemplated (see INDICATIONS) this can be accomplished by sequential intermittent intravenous infusion provided that separate secondary intravenous tubing is used, and that the primary intravenous tubing is adequately irrigated with an approved diluent between doses. It is also suggested that CEFOBID be administered prior to the aminoglycoside. *In vitro* testing of the effectiveness of drug combination(s) is recommended.

In a pharmacokinetic study, a total daily dose of 16 grams was administered to severely immunocompromised patients by constant infusion without complications. Steady-state serum concentrations were approximately 150 mcg/mL in these patients.

RECONSTITUTION

The following solutions may be used for the initial reconstitution of CEFOBID sterile powder:

Table 1. Solutions for Initial Reconstitution

5% Dextrose Injection (USP)	0.9% Sodium Chloride Injection (USP)
5% Dextrose and 0.9% Sodium Chloride Injection (USP)	Normosol® M and 5% Dextrose
5% Dextrose and 0.2% Sodium Chloride Injection (USP)	Injection
10% Dextrose Injection (USP)	Normosol® R
Bacteriostatic Water for Injection [Benzyl Alcohol or Parabens] (USP)*†	Sterile Water for Injection*

* Not to be used as a vehicle for intravenous infusion.

† Preparations containing Benzyl Alcohol should not be used in neonates.

General Reconstitution Procedures

CEFOBID sterile powder for intravenous or intramuscular use may be initially reconstituted with any compatible solution mentioned above in Table 1. Solutions should be allowed to stand after reconstitution to allow any foaming to dissipate to permit visual inspection for complete solubilization. Vigorous and prolonged agitation may be necessary to solubilize CEFOBID in higher concentrations (above 333 mg cefoperazone/mL). The maximum solubility of CEFOBID sterile powder is approximately 475 mg cefoperazone/mL of compatible diluent.

Preparation for Intravenous Use

General. CEFOBID concentrations between 2 mg/mL and 50 mg/mL are recommended for intravenous administration.

Table 2. Vehicles for Intravenous Infusion

5% Dextrose Injection (USP)	Lactated Ringer's Injection (USP)
5% Dextrose and Lactated Ringer's Injection	0.9% Sodium Chloride Injection (USP)
5% Dextrose and 0.9% Sodium Chloride Injection (USP)	Normosol® M and 5% Dextrose Injection
5% Dextrose and 0.2% Sodium Chloride Injection (USP)	Normosol® R
10% Dextrose Injection (USP)	

DIRECTIONS FOR PROPER USE OF PHARMACY BULK PACKAGE

The 10 gram vial should be reconstituted with 95 mL of sterile water for injection in two separate aliquots in a suitable work area such as a laminar flow hood. Add 45 mL of solution, shake to dissolve and add 50 mL, shake for final solution. The resulting solution will contain 100 mg/mL of cefoperazone. This closure may be penetrated only one time after reconstitution, if needed, using a suitable sterile transfer device or dispensing set which allows measured dispensing of the contents.

Discard unused solution within 24 hours of initial entry.

Reconstituted Bulk Solutions Should Not Be Used For Direct Infusion.

Although after reconstitution of the Pharmacy Bulk Package, no significant loss of potency occurs for 24 hours at room temperature and for 5 days if refrigerated, transfer individual dose to appropriate intravenous infusion solutions as soon as possible following reconstitution of the bulk package. Discard unused portions of solution held longer than these recommended periods at room temperature or under refrigeration. The stability of the solution which has been transferred into a container varies according to diluent and concentration. (See STORAGE AND STABILITY.)

The 10 gram vials may be further diluted with the parenteral diluents listed under **Table 2. Vehicles for Intravenous Infusion.** The parenteral diluents and approximate concentrations of CEFOBID that provide stable solutions are presented under STORAGE AND STABILITY.

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

STORAGE AND STABILITY

CEFOBID sterile powder is to be stored at or below 25°C (77°F) and protected from light prior to reconstitution. After reconstitution, protection from light is not necessary.

The following parenteral diluents and approximate concentrations of CEFOBID provide stable solutions under the following conditions for the indicated time periods. (After the indicated time periods, unused portions of solutions should be discarded.)

Controlled Room Temperature (15°–25°C/59°–77°F)	Approximate
24 Hours	Concentrations
Bacteriostatic Water for Injection [Benzyl Alcohol or Parabens] (USP)	300 mg/mL
5% Dextrose Injection (USP)	2 mg to 50 mg/mL
5% Dextrose and Lactated Ringer’s Injection	2 mg to 50 mg/mL
5% Dextrose and 0.9% Sodium Chloride Injection (USP)	2 mg to 50 mg/mL
5% Dextrose and 0.2% Sodium Chloride Injection (USP)	2 mg to 50 mg/mL
10% Dextrose Injection (USP)	2 mg to 50 mg/mL
Lactated Ringer’s Injection (USP)	2 mg/mL
0.5% Lidocaine Hydrochloride Injection (USP)	300 mg/mL
0.9% Sodium Chloride Injection (USP)	2 mg to 300 mg/mL
Normosol® M and 5% Dextrose Injection	2 mg to 50 mg/mL
Normosol® R	2 mg to 50 mg/mL
Sterile Water for Injection	100 mg to 300 mg/mL

Reconstituted CEFOBID solutions may be stored in glass or plastic syringes, or in glass or flexible plastic parenteral solution containers.

Refrigerator Temperature (2°–8°C/36°–46°F)	Approximate
5 Days	Concentrations
Bacteriostatic Water for Injection [Benzyl Alcohol or Parabens] (USP)	300 mg/mL
5% Dextrose Injection (USP)	2 mg to 50 mg/mL
5% Dextrose and 0.9% Sodium Chloride Injection (USP)	2 mg to 50 mg/mL
5% Dextrose and 0.2% Sodium Chloride Injection (USP)	2 mg to 50 mg/mL
Lactated Ringer’s Injection (USP)	2 mg/mL
0.5% Lidocaine Hydrochloride Injection (USP)	300 mg/mL
0.9% Sodium Chloride Injection (USP)	2 mg to 300 mg/mL
Normosol® M and 5% Dextrose Injection	2 mg to 50 mg/mL
Normosol® R	2 mg to 50 mg/mL
Sterile Water for Injection	100 mg to 300 mg/mL

Reconstituted CEFOBID solutions may be stored in glass or plastic syringes, or in glass or flexible plastic parenteral solution containers.

Freezer Temperature (–20° to –10°C/–4° to 14°F)	Approximate
3 Weeks	Concentrations
5% Dextrose Injection (USP)	50 mg/mL
5% Dextrose and 0.9% Sodium Chloride Injection (USP)	2 mg/mL
5% Dextrose and 0.2% Sodium Chloride Injection (USP)	2 mg/mL

5 Weeks

0.9% Sodium Chloride Injection (USP)	300 mg/mL
Sterile Water for Injection.	300 mg/mL

Reconstituted CEFOBID solutions may be stored in plastic syringes, or in flexible plastic parenteral solution containers.

Frozen samples should be thawed at room temperature before use. After thawing, unused portions should be discarded. Do not refreeze.

HOW SUPPLIED

CEFOBID® sterile powder is available in Pharmacy Bulk Package containing cefoperazone sodium equivalent to 10 g cefoperazone × 1 (NDC 0049-1219-28).

OTHER SIZE PACKAGES AVAILABLE

CEFOBID® sterile powder is available in vials containing cefoperazone sodium equivalent to 1 g cefoperazone × 10 (NDC 0049-1201-83) and 2 g cefoperazone × 10 (NDC 0049-1202-83) for intramuscular and intravenous administration.

Rx only



Distributed by

Roerig

Division of Pfizer Inc, NY, NY 10017

LAB-0034-3.0
Revised January 2006