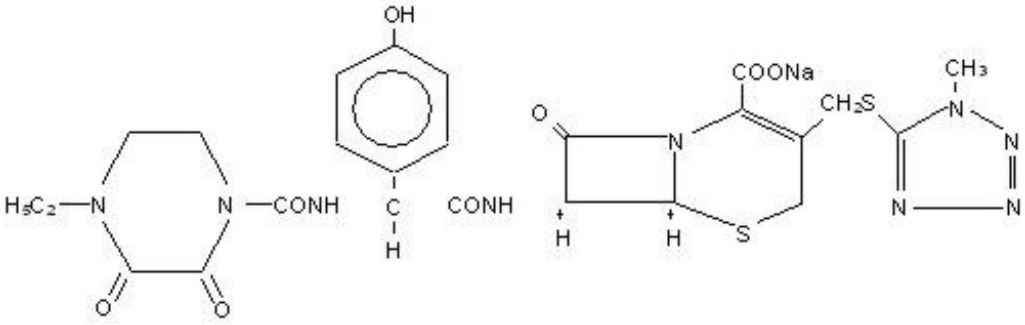
CEFOBID- cefoperazone powder, for solution
Roerig

CEFOBID®
(sterile cefoperazone)
Formerly known as sterile cefoperazone sodium
For Intravenous or Intramuscular Use

DESCRIPTION

CEFOBID® (sterile cefoperazone), formerly known as sterile cefoperazone sodium, contains cefoperazone as cefoperazone sodium. It is a semisynthetic, broad-spectrum cephalosporin antibiotic. Chemically, cefoperazone sodium is sodium (6*R*,7*R*)-7-[(*R*)-2-(4-ethyl-2,3-dioxo-1-piperazinecarboxamido)-2-(*p*-hydroxyphenyl)- acetamido-3-[[(1-methyl-1*H*-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate. Its molecular formula is $C_{25}H_{26}N_9NaO_8S_2$ with a molecular weight of 667.65. The structural formula is given below:



CEFOBID (sterile cefoperazone) 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 (sterile cefoperazone) in crystalline form is supplied in vials containing 1 g or 2 g cefoperazone as cefoperazone sodium for intravenous or intramuscular administration.

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

	Mean Serum Concentrations (mcg/mL)						
Dose/Route	**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.

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

Microbiology

CEFOBID is active *in vitro* against a wide range of aerobic and anaerobic, gram-positive and gram-negative pathogens. The bactericidal action of CEFOBID results from the inhibition of bacterial cell wall synthesis. CEFOBID has a high degree of stability in the presence of beta-lactamases produced by

most gram-negative pathogens. CEFOBID is usually active against organisms which are resistant to other beta-lactam antibiotics because of beta-lactamase production. CEFOBID 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 organism/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 MICs 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

CEFOBID 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*[1] (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*,[1] and anaerobic gram-negative bacilli (including *Bacteroides fragilis*).

Bacterial Septicemia caused by *S. pneumoniae, S. agalactiae,[1] S. aureus, Pseudomonas aeruginosa,[1] E. coli, Klebsiella* spp.,[1]*Klebsiella pneumoniae,[1] Proteus* species[1] (indole-positive and indole-negative), *Clostridium* spp.[1] and anaerobic gram-positive cocci.[1]

Infections of the Skin and Skin Structures caused by *S. aureus* (penicillinase and non-penicillinase producing strains), *S. pyogenes*,[1] and *P. aeruginosa.*

Pelvic Inflammatory Disease, Endometritis, and Other Infections of the Female Genital Tract caused by *N. gonorrhoeae, S. epidermidis,[1] S. agalactiae, E. coli, Clostridium* spp.,[1]*Bacteroides* species (including *Bacteroides fragilis*), and anaerobic gram-positive cocci.

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**,[1] 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.

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1 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.

CEFOBID is extensively excreted in bile. The serum half-life of CEFOBID 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 CEFOBID (see CLINICAL PHARMACOLOGY), patients with renal failure require no adjustment in dosage when usual doses are administered. When high doses of CEFOBID 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 CEFOBID 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, CEFOBID 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.

CEFOBID 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 CEFOBID animal toxicity studies is six months. In none of the *in vivo* or *in vitro* genetic toxicology studies did CEFOBID show any mutagenic potential at either the chromosomal or subchromosomal level. CEFOBID 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. CEFOBID 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

The usual adult daily dose of CEFOBID (sterile cefoperazone) 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.

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.

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

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.

RECONSTITUTION

The following solutions may be used for the initial reconstitution of CEFOBID (sterile cefoperazone).

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 Injection
5% Dextrose and 0.2% Sodium Chloride Injection (USP)	Normosol® R
10% Dextrose Injection (USP)	Sterile Water for Injection*
Bacteriostatic Water for Injection [Benzyl Alcohol	

Bacteriostatic Water for Injection [Benzyl Alcohol or Parabens] (USP)*†	

* 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 cefoperazone) 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 cefoperazone) is approximately 475 mg cefoperazone/mL of compatible diluent.

Preparation for Intravenous Use

General

CEFOBID (sterile cefoperazone) concentrations between 2 mg/mL and 50 mg/mL are recommended for intravenous administration.

Preparation of Vials

Vials of CEFOBID (sterile cefoperazone) may be initially reconstituted with a minimum of 2.8 mL per gram of cefoperazone of any compatible reconstituting solution appropriate for intravenous administration listed above in Table 1. For ease of reconstitution the use of 5 mL of compatible solution per gram of CEFOBID is recommended. The entire quantity of the resulting solution should then be withdrawn for further dilution and administration using any of the following vehicles for intravenous infusion:

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)	

The resulting intravenous solution should be administered in one of the following manners:

Intermittent Infusion

Solutions of CEFOBID should be administered over a 15–30 minute time period.

Continuous Infusion

CEFOBID can be used for continuous infusion after dilution to a final concentration of between 2 and 25 mg cefoperazone per mL.

Preparation for Intramuscular Injection

Any suitable solution listed above may be used to prepare CEFOBID (sterile cefoperazone) for intramuscular injection. When concentrations of 250 mg/mL or more are to be administered, a lidocaine solution should be used. These solutions should be prepared using a combination of Sterile Water for Injection and 2% Lidocaine Hydrochloride Injection (USP) that approximates a 0.5% Lidocaine

Hydrochloride Solution. A two-step dilution process as follows is recommended: First, add the required amount of Sterile Water for Injection and agitate until CEFOBID powder is completely dissolved. Second, add the required amount of 2% lidocaine and mix.

	Final Cefoperazone Concentration	Step 1 Volume of Sterile Water	Step 2 Volume of 2% Lidocaine	Withdrawable Volume*†
1 g vial	333 mg/mL	2.0 mL	0.6 mL	3 mL
	250 mg/mL	2.8 mL	1.0 mL	4 mL
2 g vial	333 mg/mL	3.8 mL	1.2 mL	6 mL
	250 mg/mL	5.4 mL	1.8 mL	8 mL

* There is sufficient excess present to allow for withdrawal of the stated volume.

† Final lidocaine concentration will approximate that obtained if a 0.5% Lidocaine Hydrochloride Solution is used as diluent.

When a diluent other than Lidocaine HCl Injection (USP) is used reconstitute as follows:

	Cefoperazone Concentration	Volume of Diluent to be Added	Withdrawable Volume*
1 g vial	333 mg/mL	2.6 mL	3 mL
	250 mg/mL	3.8 mL	4 mL
2 g vial	333 mg/mL	5.0 mL	6 mL
	250 mg/mL	7.2 mL	8 mL

* There is sufficient excess present to allow for withdrawal of the stated volume.

STORAGE AND STABILITY

CEFOBID (sterile cefoperazone) 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.)

Room Temperature (15°–25°C/59°–77°F)	
24 Hours	**Approximate 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	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)	
5 Days	**Approximate 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	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)	
3 Weeks	**Approximate 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 cefoperazone) 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.

CEFOBID (sterile cefoperazone) is available in 10 g (NDC 0049-1219-28) Pharmacy Bulk Package for intravenous administration.

Rx only

Distributed by

Roerig
Division of Pfizer Inc, NY, NY 10017

LAB-0033-5.0

CEFOBID

cefoperazone powder, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG LABEL	**Item Code (Source)**	NDC:0049-1201
Route of Administration	INTRAVENOUS	**DEA Schedule**	

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
cefoperazone (cefoperazone)		1 g

Inactive Ingredients	
Ingredient Name	**Strength**
sodium	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0049-1201-83	10 in 1 PACKAGE		

CEFOBID

cefoperazone powder, for solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG LABEL	**Item Code (Source)**	NDC:0049-1202
Route of Administration	INTRAVENOUS	**DEA Schedule**	

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
cefoperazone (cefoperazone)		2 g

Inactive Ingredients	
Ingredient Name	**Strength**
sodium	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:0049-1202-83	10 in 1 PACKAGE		

Labeler - Roerig

Revised: 4/2006 Roerig