

Cefoperazone and Sulbactam

Introduction: It is of Semi Synthetic origin and belongs to Cephem Carboxylate. It belongs to Peptidoglycan synthesis inhibitor pharmacological group on the basis of mechanism of action and also classified in Antibiotic, Cephalosporin-3rd Gen pharmacological group.

Mechanism of action: Cefoperazone, a third generation Cephalosporin acts by inhibiting biosynthesis of cell wall mucopeptide. Sulbactam acts a beta-lactamase inhibitor, thus restoring Cefoperazone activity against beta-lactamase producing strains.

Pharmacology:

Absorption: The mean serum concentration obtained at 30 min after 1 g I.V. Cefoperazone is 114 mcg/ml. The mean serum concentration obtained at 15 min. after 500 mg and 1000 mg IV Sulbactam are 21-40 mcg/ml and 48-88 mcg/ml respectively. The average peak plasma concentration at 5 minutes after intravenous dose of 1g is 81mg/litre.

Distribution: The protein binding of Cefoperazone is 82-93% and that of Sulbactam is 38%.

Metabolism and Excretion: No significant quantity of metabolites of Cefoperazone has been found in the urine. Cefoperazone is excreted mainly in the bile. About 75-85% of Sulbactam is excreted in the urine during the first eight hours of administration.

Pharmacokinetics in Special Groups

Renal Insufficiency in Patients: No significant changes observed compared to normal patients.

Hepatic Insufficiency Patients: In patients with hepatic dysfunction, the serum half life is prolonged and urinary excretion is increased. In patients combined with renal and hepatic insufficiency, Cefoperazone may accumulate in the serum.

Indications:

- **Monotherapy** Sulbactam/Cefoperazone is indicated for the treatment of the following infections when caused by susceptible organisms:
 - Respiratory Tract Infections (Upper and Lower)
 - Urinary Tract Infections (Upper and Lower)
 - Peritonitis, Cholecystitis, Cholangitis, and Other Intra-Abdominal Infections
 - Septicemia – Meningitis
 - Skin and Soft Tissue Infections
 - Bone and Joint Infections
 - Pelvic Inflammatory Disease, Endometritis, Gonorrhoea, and Other Infections of the Genital Tract
- **Combination Therapy** Because of the broad spectrum of activity of sulbactam/cefoperazone, most infections can be treated adequately with there antibiotic alone. However, Sulbactam/Cefoperazone may be used concomitantly with other antibiotics if such combinations are indicated. If an aminoglycoside is used, renal function should be monitored during the course of therapy.

Dosage: Daily dosage recommendations for sulbactam/cefoperazone in adults are as follows:

Ratio of Sulbactam: Cefoperazone	SBT/CPZ (g)	Sulbactam (g)	Cefoperazone (g)
1:1	2.0–4.0	1.0–2.0	1.0–2.0

Doses should be administered every 12 hours in equally divided doses.

- In severe or refractory infections the daily dosage of sulbactam/cefoperazone may be increased up to 8 g of the 1:1 ratio (i.e., 4 g cefoperazone activity). Patients receiving the 1:1 ratio may require additional cefoperazone administered separately. Doses should be administered every 12 hours in equally divided doses. The recommended maximum daily dosage of sulbactam is 4 g.
- *Use in Children* Daily dosage recommendations for sulbactam/cefoperazone in children are as follows:

Ratio of Sulbactam: Cefoperazone	SBT/CPZmg/kg /day	Sulbactammg/kg /day	Cefoperazonemg/k g/day
1:1	40–80	20–40	20–40

Doses should be administered every 6 to 12 hours in equally divided doses.

In serious or refractory infections, these dosages may be increased up to 160 mg/kg/day. Doses should be administered in two to four equally divided doses.

- *Use in Neonates* For neonates in the first week of life, the drug should be given every 12 hours. The maximum daily dosage of sulbactam in pediatrics should not exceed 80 mg/kg/day. If more than 80 mg/kg/day of Cefoperazone activity are necessary, additional Cefoperazone should be administered
- *Reconstitution* Sulbactam/Cefoperazone is available in 1.0 g vial.

Total dosage (g)	Equivalent dosage of Sulbactam + Cefoperazone (g)	Volume of diluent conc. (ml)	Maximum final dose of Sulbactam+Cefoperazone (mg/ml)
1.0	0.5 + 0.5	3.4	125 + 125

Sulbactam/Cefoperazone has been shown to be compatible with water for injection, 5% dextrose, normal saline, 5% dextrose in 0.225% saline, and 5% dextrose in normal saline.

- **Intravenous Administration** For intravenous infusion, each vial of Sulbactam/Cefoperazone should be reconstituted with the appropriate amount of 5% Dextrose in water, 0.9% Sodium chloride solution or Sterile water for injection and then diluted to 20 ml with the same solution followed by administration over 15 to 60 minutes. Lactated Ringer's solution is a suitable vehicle for intravenous infusion, however, not for initial reconstitution. For intravenous injection, each vial should be reconstituted as above and administered over a minimum period of 3 minutes.

Side effects:

Hypersensitivity: 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 have been reported. Decreased hemoglobins or hematocrits have been reported, which is consistent with published literature on other cephalosporins. **Gastrointestinal:** Diarrhea or loose stools has been reported. 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.

Precautions:

Local Reactions: Cefoperazone is well tolerated following intramuscular administration. Occasionally, transient pain may follow administration by this route. When Cefoperazone is administered by intravenous infusion some patients may develop phlebitis at the infusion site.

Pregnancy: Cefoperazone should be used during pregnancy only if clearly needed.

Nursing Mothers: Although cefoperazone passes poorly into breast milk of nursing mothers, caution should be exercised when cefoperazone is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established. **Geriatric Use:** 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.

Contraindication:

Cefoperazone is contraindicated in patients with known allergy to penicillins or any of the Cephalosporin.

How supplied: Customized as per request.