PRODUCT MONOGRAPH

FOR

EFOBACT-SM

(Cefoperazone Sodium and Sulbactam Sodium Injection 1.5 g)

For IV/IM Use

Efobact-TZ (Cefoperazone and Sulbactam Injection 1.5g) should be used only to treat infections that are proven or strongly suspected to be caused by bacteria in order to reduce the development of drug-resistant bacteria and maintain the effectiveness of Cefoperazone and other antibacterial drugs.

Cefoperazone for injection is a semi synthetic 3rd generation Cephalosporin intended for intravenous administration. It belongs to Peptidoglycan synthesis inhibitor pharmacological group on the basis of mechanism of action. Sulbactam is an antibiotic of the beta-lactamase inhibitor class that prevents the breakdown of other antibiotics by beta-lactamase enzyme producing organisms.

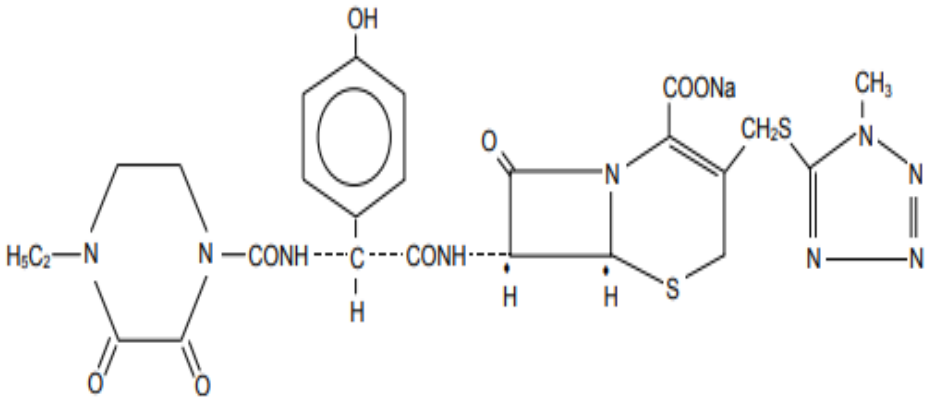
Cefoperazone & Sulbactam Injection - Composition and Active Ingredients

Each vial contains:

1. Cefoperazone Sodium IP (Eq. to Cefoperazone 1000mg)
2. Sulbactam Sodium (Eq. to Sulbactam 500mg)

DESCRIPTION

Cefoperazone is a semi-synthetic, broad-spectrum cephalosporin antibacterial drug. Chemically, Cefoperazone sodium is sodium (6R,7R)-7-[(R)-2-(4-ethyl-2,3 dioxo-1-piperazinecarboxamido)-2-(p-hydroxyphenyl)-acetamido-3-[[(1-methyl-1H-tetrazol-5thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate. Its molecular formula is C25H26N9NaO8S2 with a molecular weight of 667.65. The structural formula is given below:



MECHANISM OF ACTION

Cefoperazone, a bactericidal antimicrobial, inhibits bacterial cell wall synthesis of actively dividing cells by binding to one or more penicillin-binding proteins (PBPs). These proteins are associated with the bacterial cell membrane and probably serve in synthesis. The result is the formation of a defective cell wall that is osmotically unstable resulting into bacterial lysis.

Sulbactam is a penicillinate sulfone. Being a beta-lactamase inhibitor, it is synergistic with many beta-lactamase labile drugs such as penicillins and cephalosporin's. Sulbactam inhibits all beta-lactamases inhibited by Clavulanic acid, but, in addition, it also has some activity against chromosomally-mediated induced (or derepressed) enzymes of Morganella morganii, Citrobacter freundii, Enterobacter cloacae, Serratia marcescens and Pseudomonas aeruginosa. Sulbactam also appears to be a weaker enzyme inducer than other beta-lactamase inhibitors.

Combination of Sulbactam &Cefoperazone: The combination of Sulbactam and cefoperazone is a useful combination for the treatment of infection due to extended-spectrum beta-lactamase (ESBL) producing organisms.

PHARMACOLOGY

Pharmacodynamics

The antibacterial component of Cefoperazone is cefoperazone, a third-generation cephalosporin, which acts against sensitive organisms during the stage of active multiplication by inhibiting the biosynthesis of cell wall mucopeptide.

Sulbactam is metabolized to a single metabolite that lacks pharmacological and antibacterial activities. Sulbactam is eliminated via the kidneys by glomerular filtration and tubular secretion. Sulbactam and its metabolite are eliminated primarily by renal excretion, with 80% of the administered dose excreted as unchanged drug and the remainder as a single metabolite. Sulbactam is also secreted into the bile. Sulbactam is approximately 30% bound to plasma proteins. Protein binding of the Sulbactam metabolite is negligible. Sulbactam is widely distributed to tissues and body fluids, including the intestinal mucosa, gall bladder, lungs, female reproductive tissues (uterus, ovary and fallopian tube), interstitial fluid, and bile.

Pharmacokinetics

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. Tazobactam is mainly metabolized to M1, an inactive metabolite. Hydrolysis occurs on the beta-lactam ring to form M1 (the inactive metabolite). Within one-hour peak plasma concentration of 15.6 mcg/mL for tazobactam, is attained. The absolute bioavailability (F) was 84% for tazobactam.

Metabolism and Excretion:

No significant quantity of metabolites of Cefoperazone has been found in the urine. Cefoperazone is excreted mainly in the bile. Tazobactam and its metabolite are mainly eliminated by the kidneys with about 80% of the administered dose eliminated as unchanged drug. The remaining drug is excreted as a single metabolite.

DOSAGE AND ADMINISTRATION

Adults **:**2-4gm daily in equally divided dosage (Doses should be administered every 12 hours in equally divided doses)

Pharmacokinetics In Special Groups

Renal Insufficiency in Patients: The mean clearance rate of tazobactam was found to be 48.3-83.6 mL/min in patients admitted to the intensive care unit who were given renal replacement therapy and hence we have to consider that the clearance of tazobactam is dependent on renal function, as determined by renal clearance. However, cefoperazone does not require any dose adjustment.

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

Cefoperazone & Tazobactam Injection is used for the treatment, control, prevention, & improvement of the following diseases, conditions and symptoms:

- Bacterial Infection of the Respiratory Tract
- Peritonitis

- Urinary Tract Infection
- Endometritis
- Pelvic Inflammatory Disease
- Septicemia
- Bacterial Infections of Urinary Tract
- Bacterial Infections of Bones and Joint Infections
- Bacterial Infections of Vagina
- Bacterial Infections of Stomach
- Bacterial Infections of Skin
- Bacterial Infections of Pneumonia

CONTRAINDICATIONS

It is contraindicated in patients with a known allergy to penicillins, sulbactam, cefoperazone, or any of the cephalosporins.

WARNINGS AND PRECAUTIONS

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving beta-lactam or cephalosporin therapy. If an allergic reaction occurs, the drug should be discontinued and the appropriate therapy instituted. Serious anaphylactic reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should be administered as indicated.

DRUG INTERACTIONS

A reaction characterized by flushing, sweating, headache and tachycardia has been reported when alcohol was ingested during and as late as the fifth day after Cefoperazone administration. A similar reaction has been reported with certain other cephalosporins and patients should be cautioned concerning ingestion of alcoholic beverages in conjunction with administration of Tazobactam/ Cefoperazone. For patients requiring artificial feeding orally or parenterally, solutions containing ethanol should be avoided.

Pregnancy

Tazobactam has been found cross the placenta in rats. No data on human studies are available, however, rat studies have shown no teratogenic effects at doses 6-14 times the equivalent maximum recommended human dose.

Lactation

There are no data on the presence of tazobactam in human breast milk. No data are currently available on the effects of tazobactam on the infant, or how it affects milk production. Use clinical judgment and consider the maternal need for the drug and the benefits of breastfeeding the infant before administration during lactation.

SIDE EFFECTS

The following is a list of possible side effects that may occur from all constituting ingredients of Cefoperazone & Tazobactam Injection. This is not a comprehensive list. These side effects are possible, but do not always occur. Some of the side effects may be rare but serious. Consult your doctor if you observe any of the following side effects, especially if they do not go away.

- Decrease in White Blood Cells
- Decrease in Hemoglobin
- Nausea
- Vomiting
- Transient Increases in Urea Nitrogen
- Creatinine Levels in Blood

OVERDOSAGE

Overdosage of the drug would be expected to produce manifestations that are principally extensions of the adverse reactions reported with the drug. The fact that high CSF concentrations of B-lactam antibiotics may cause neurologic effects, including seizures, should be considered. Because Cefoperazone and Tazobactam are both removed from the circulation by hemodialysis, these procedures may enhance elimination of the drug from the body if overdosage occurs in patients with impaired renal function

INTRAVENOUS ADMINISTRATION

Reconstitution

Dissolve the contents with 10mL of sterile water for injections IP for IV use and 3.8 mL of sterile water for Injections for IM use. For IV further dilution is required administer for 15-30 mins

STORAGE AND HANDLING INSTRUCTIONS

Store in a cool, dry & dark place at a temperature not exceeding 30ºC, protected from light.

Reconstituted Solution

0.9% NaCl, 5% Dextrose or Lactated ringer's solution

HOW SUPPLIED

Efobact-TZ (Cefoperazone and Tazobactam Injection 1.125g) is available in 1.125 g in glass vial.

REFERENCES

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