ROSOBAC-1GM / ROSOBAC-FORTE

FOR I.V./I.M. USE ONLY

COMPOSITION

ROSOBAC - 1GM

Each vial contains
Sterile Cefoperazone Sodium IP
Eq. to Anhydrous Cefoperazone - 500mg.
Sterile Sulbactum Sodium USP
Eq. to Anhydrous Sulbactum - 500mg.

ROSOBAC - FORTE

Each vial contains
Sterile Cefoperazone Sodium IP
Eq. to Anhydrous Cefoperazone - 1000mg.
Sterile Sulbactum Sodium USP
Eq. to Anhydrous Sulbactum- 500mg.

DESCRIPTION :

Cefoperazone sodium is a semi-synthetic broad-spectrum cephalosporin antibiotic for parenteral use only. Cefoperazone is a white crystalline powder which is freely soluble in water. The chemical formula is $C_{25}H_{27}N_9O_8S_2$.

Sulbactum sodium is a derivative of the basic penicillin nucleus. It is an irreversible beta-lactamase inhibitor for parenteral use only. Chemically it is sodium penicillinate sulfone. Sulbactum is an off-white crystalline powder which is highly soluble in water. The chemical formula is $C_8H_{11}NO_5S$.

PHARMACOLOGY :

Pharmacodynamics :

The anti-bacterial activity exert by Cefoperazone in the composition of cefoperazone/Sulbactum, as cefoperazone is a third generation cephalosporin, which acts against sensitive organisms during the stage of active multiplication by inhibiting biosynthesis of cell wall mucopeptide.

Sulbactum does not possess any useful antibacterial activity, except against Neisseriaceae and Acinetobacter. However, biochemical studies with cell-free bacterial systems have shown it to be an irreversible inhibitor of most important beta-lactamases produced by beta-lactam antibiotic-resistant organisms. Sulbactum exhibited significant synergy efficacy with penicillins and cephalosporins. As Sulbactum also binds with some penicillin binding proteins, sensitive strains are also often rendered more susceptible to cefoperazone/Sulbactum than to cefoperazone alone. The combination of Sulbactum and cefoperazone is active against all organisms sensitive to cefoperazone.

Pharmacokinetics :

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

Distribution: The protein binding of Cefoperazone is 82-93% and that of Sulbactum 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 Sulbactum is excreted in the urine during the first eight hours of administration.

Renal Insufficiency 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:

Because of the broad spectrum of activity of Cefoperazone/Sulbactum, most infections can be treated adequately with this antibiotic combination alone. However, Cefoperazone/Sulbactum may also 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. Cefoperazone/Sulbactum combined therapy can effectively tackle the followings conditions :

i. Respiratory tract infections (upper and lower).
ii. Urinary tract infections (upper and lower).
iii. Peritonitis, cholecystitis, cholangitis, and other intra-abdominal infections.
iv. Septicaemia.
v. Meningitis.
vi. Skin and soft tissue infections.
vii. Bone and joint infections.
viii. Pelvic inflammatory disease, endometritis, gonorrhoea, and other infections of the genital tract.

CONTRAINDICATIONS :

It is contraindicated in patients with a known allergy to penicillins, Sulbactum, 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. These reactions are more prompt to occur in individuals with a history of hypersensitivity reactions to multiple allergens. If an allergic reaction occurs, the drug should be discontinued and the appropriate therapy must be instituted. As with other antibiotics, overgrowth of non-susceptible organisms may occur during the prolonged use of Cefoperazone/Sulbactum.

Neonates : It has not been extensively studied in premature infants or neonates. Therefore, in treating premature infants and neonates, the potential benefits and possible risks involved should be considered before instituting therapy.

Hepatic Impairment : In severe hepatic dysfunction, therapeutic concentrations of Cefoperazone are obtained in the bile and only a 2-to 4-fold increase in the half-life is seen. Dose modification may be necessary in case of severe biliary obstruction, severe hepatic disease or in case of renal dysfunction coexistent with either of those conditions.

Pregnancy : There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

Lactation : Caution should be exercised when Cefoperazone /Sulbactum is administered to a nursing mother.

DRUG INTERACTION :

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 Cefoperazone/Sulbactum. For patients requiring artificial feeding orally or parenterally, solutions containing ethanol should be avoided.

SIDE EFFECTS :

Cefoperazone/Sulbactum is generally well-tolerated. The majorities of adverse events is of mild or moderate severity and are tolerated with continued treatment. The most frequent side effects observed with Cefoperazone/Sulbactum have been gastrointestinal. Other adverse reactions include dermatologic reactions, headache, injection pain, chills, and anaphylactoid reactions.

OVERDOSAGE :

Limited information is available on the acute toxicity of Cefoperazone Sodium and Sulbactum Sodium in humans. Over dosage of the drug would be expected to produce manifestations that are principally extensions of the adverse reactions reported with the drug.

DOSAGE AND ADMINISTRATION :

Adults : The usual adult dose of the combination is 2 to 4 g/day (i.e, 1-2 g/day each of Cefoperazone and Sulbactum) given IV or IM in equally divided doses every 12 hours. In severe or refractory infections the daily dosage may be increased to 8g (i.e, 4g/day each of Cefoperazone and Sulbactum) given IV in equally divided doses every 12 hours. The recommended maximum daily dosage of Sulbactum is 4g (8g of the combination).

Children : The usual dosage in children is 40-80mg/kg/day (20 to 40 mg/kg/day each of Cefoperazone and Sulbactum) every six to twelve hours. In serious or refractory infections, these dosages may be increased up to 240mg/kg/day (160 mg/kg/day cefoperazone activity). 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 Sulbactum in paediatrics should not exceed 80 mg/kg/day.

Renal Impairment : Dosage regimens of Cefoperazone /Sulbactum should be adjusted in patients with a marked decrease in renal function (creatinine clearance of less than 30 ml/min) to compensate for the reduced clearance of Sulbactum. Patients with creatinine clearances between 15 and 30 ml/min should receive a maximum of 1 g of Sulbactum every 12 hours (maximum daily dosage of 2 g Sulbactum), while patients with creatinine clearances of less than 15 ml/min should receive a maximum of 500 mg of Sulbactum every 12 hours (maximum daily dosage of 1 g Sulbactum). The pharmacokinetic profile of Sulbactum is significantly altered by haemodialysis. The serum half-life of cefoperazone is reduced slightly during haemodialysis. Thus, dosing should be scheduled to follow a dialysis period.

Hepatic Impairment : Cefoperazone is extensively excreted through the bile. Dose modification may be necessary in cases of severe biliary obstruction, severe hepatic disease or in cases of renal dysfunction coexistent with either of those conditions. In such cases, dosage should not exceed 2 g/day of cefoperazone without close monitoring of serum concentrations.

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

RECONSTITUTION :

For intravenous infusion, each vial of Sulbactum/Cefoperazone should be reconstituted with the appropriate amount of 5% Dextrose, 0.9% Sodium Chloride Injection or Sterile Water for Injection, then further diluted to 20 ml with the same solution, and followed by administration over 15 to 60 minutes. Lactated Ringer's Solution is a suitable vehicle for intravenous infusion, but it is not, however, for initial reconstitution. For intravenous injection, each vial should be reconstituted as above and administered over a minimum of 3 minutes.

Intramuscular Administration Lidocaine HCl 2% is a suitable vehicle for intramuscular administration; however, it is not for initial reconstitution.

INCOMPATIBILITY :

Aminoglycosides - Solutions of Cefoperazone/Sulbactum and aminoglycosides should not be directly mixed, since there is a physical incompatibility between them.

Lactated Ringer's - Solution Initial reconstitution with Lactated Ringer's Solution should be avoided since this mixture has been shown to be incompatible. However, a two-step dilution process involving initial reconstitution in Sterile Water for Injection will result in a compatible mixture when further diluted with Lactated Ringer's Solution.

STORAGE AND HANDLING INSTRUCTIONS :

Store below 25°C. Protect from light. Keep out of reach of children. Reconstituted Solution Reconstituted solution is stable for 7 days at 2-8°C and for 24 hours at 8-25°C.

HOW SUPPLIED :

Glass vial with diluents in a carton.