Biocon

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Cefoperazone & Sulbactam for Injection 1g/1.5g/2g

CEGAVA® 1g/1.5g/2g सेगावा १जी/१.५जी/२ जी

COMPOSITION
CEGAVA® 1g
Each Vial contains:
Cefoperazone Sodium I.P. (Sterile)
Eq. to Cefoperazone 500 mg
Sulbactam Sodium I.P. (Sterile)
Eq. to Sulbactam 500 mg

CEGAVA® 1.5g
Each Vial contains:
Cefoperazone Sodium I.P. (Sterile)
Eq. to Cefoperazone 1000 mg
Sulbactam Sodium I.P. (Sterile)
Eq. to Sulbactam 500 mg

CEGAVA® 2g
Each Vial contains:
Cefoperazone Sodium I.P. (Sterile)
Eq. to Cefoperazone 1000 mg
Sulbactam Sodium I.P. (Sterile)
Eq. to Sulbactam 1000 mg

Pharmaceutical form: Powder for reconstitution (IV/IM use only).

ATC code: J01DD62

DESCRIPTION
The Sulbactam Sodium and Cefoperazone Sodium combination consists of a beta-lactamase inhibitor plus a beta lactam antibiotic. This sulbactam /cefoperazone combination is available as a dry powder .

PHARMACOLOGY
Pharmacodynamics
The antibacterial component of Sulbactam/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 does not possess any useful antibacterial activity, except against Neisseriaceae and Acinetobacter. As sulbactam also binds with some penicillin-binding proteins, sensitive strains are also often rendered more susceptible to Sulbactam/ Cefoperazone than to Cefoperazone alone.

The combination of Sulbactam and Cefoperazone is active against all organisms sensitive to cefoperazone. In addition, it demonstrates synergistic activity (up to 4-fold reduction in the minimum inhibitory concentrations for the combination versus those for each component) in a variety of organisms.

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

Combination Therapy
Because of the broad spectrum of activity of Sulbactam/Cefoperazone, most infections can be treated adequately with this antibiotic combination alone. However, Sulbactam/Cefoperazone 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.

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. These reactions are more apt 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 instituted.

As with other antibiotics, overgrowth of non-susceptible organisms may occur during the prolonged use of Sulbactam/Cefoperazone. 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.

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

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. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

For the use only of a Registered Medical Practitioner or Hospital or Laboratory

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

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

OVERDOSAGE
Limited information is available on the acute toxicity of Cefoperazone Sodium and Sulbactam Sodium in humans. Overdosage 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 Sulbactam) given IV or IM in equally divided doses every 12 hours. In severe or refractory infections the daily dosage may be increased to 8 g (i.e, 4 g/day each of Cefoperazone and Sulbactam) given IV in equally divided doses every 12 hours. The recommended maximum
daily dosage of Sulbactam is 4 g (8 g of the combination).

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

Renal Impairment
Dosage regimens of sulbactam/cefoperazone 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 sulbactam. Patients with creatinine clearances between 15 and 30 mL/min should receive a maximum of 1 g of sulbactam every 12 hours (maximum daily dosage of 2 g sulbactam), while patients with creatinine clearances of less than 15 mL/min should receive a maximum of 500 mg of sulbactam every 12 hours (maximum daily dosage of 1 g sulbactam). The pharmacokinetic profile of sulbactam 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.

Intravenous Administration
Reconstitution
For intravenous infusion, each vial of Cefoperazone and Sulbactam powder should be reconstituted with the appropriate amount of 5% Dextrose and 0.9% Sodium Chloride Injection or Sterile Water for Injections IP, 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, however it is not for initial reconstitution.

For intravenous injection, each vial should be reconstituted as above and administered over a minimum of 3 minutes.

Intramuscular Administration
After initial reconstitution Lidocaine HCL 2 % can be added for Intramuscular adminstration.

INCOMPATIBILITY
Aminoglycosides
Solutions of sulbactam/cefoperazone 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 Injections IP will result in a compatible mixture when further diluted with Lactated Ringer's Solution.

Shelf life: Please refer to carton/ label.

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°C - 8°C and for 24 hours at 8°C - 25°C.

How supplied
Glass vial in a carton

Marketed by:
Biocon Biologics India Limited
Biocon House, Semicon Park,
Electronics City, Phase - II,
Bengaluru - 560 100, India.

® - Registered trademark

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To report adverse events and/or product complaints visit our website **www.biocon.com** or call toll free No: **1800 102 9465** or e mail us at **drugsafety@biocon.com**

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