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

Cefoperazone & Sulbactam for Injection

Galencef-S Forte

COMPOSITION
Each combipack contains:
(A) 1 Vial of Cefoperazone & Sulbactam for Injection
Each vial contains :
Cefoperazone Sodium IP (Sterile) eq. to Anhydrous Cefoperazone 2 gm
Sulbactam Sodium IP (Sterile) eq. to Sulbactam 1 gm
(B) 1 Ampoule of Sterile Water for Injections IP
Each ampoule contains:
Sterile Water for Injections IP 10 ml

DESCRIPTION
The sulbactam sodium and cefoperazone sodium combination consists of a beta-lactamase inhibitor plus a beta-lactam. This sulbactam/cefoperazone combination is available as a dry powder for reconstitution in a 1:2 ratio.

PHARMACOKINETIC PROPERTIES
A third generation Cephalosporin acts by inhibiting biosynthesis of cell wall mucopeptide. Sulbactam acts as beta-lactamase inhibitor, thus restoring Cefoperazone activity against beta-lactamase producing strains.
The potential for sulbactam preventing the destruction of penicillins and cephalosporins by resistant organisms was confirmed in whole-organism studies using resistant strains in which sulbactam exhibited marked synergy with penicillins and cephalosporins. 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 cefoperazone and sulbactam 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
Approximately 84% of the Sulbactam dose and 25% of the Cefoperazone dose administered as Sulbactam / Cefoperazone is excreted by the kidneys. Most of the remaining dose of Cefoperazone is excreted in the bile. After Sulbactam / Cefoperazone administration, the mean half-life for Sulbactam is about 1 hour while that for Cefoperazone is 1.7 hours. Serum concentrations have been shown to be proportional to the dose administered. These values are consistent with previously published values for these agents when given alone.
After intramuscular administration of 3 gm Cefoperazone Sulbactam (1 gm Sulbactam, 2 gm Cefoperazone) peak serum concentrations of Sulbactam and Cefoperazone are seen from 15 minutes to 2 hours after administration. Mean peak serum concentrations were 19.0 and 64.2 mcg /mL for Sulbactam and Cefoperazone, respectively. Both Sulbactam and Cefoperazone distribute well into a variety of tissues and fluids, including the bile, gall bladder, skin, appendix, fallopian tubes, ovary, uterus, and others.

INDICATIONS
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; Septicaemia; Meningitis; Skin and soft tissue infections; Bone and joint infections; Pelvic inflammatory disease, endometritis, gonorrhoea, and other infections of the genital tract.

DOSAGE AND ADMINISTRATION
Adults
Daily dosage recommendations for Sulbactam / Cefoperazone in adults are as follows:

Ratio	Sulbactam/ Cefoperazone (g)	Sulbactam activity (g)	Cefoperazone activity (g)
1:2	3.0–6.0	1.0–2.0	2.0–4.0

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 of cefoperazone activity) or 12 g of the 1:2 ratio (i.e. 8 g of 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.
In febrile neutropenia, total daily dose can be administered twice or thrice a day in equally divided doses.
Paediatric Use
Daily dosage recommendations for Sulbactam / Cefoperazone in children are as follows:

Ratio	Sulbactam/ Cefoperazone mg/kg/day	Sulbactam activity mg/kg/day	Cefoperazone activity mg/kg/day
1:1	40–80	20–40	20–40
1:2	60–120	20–40	40–80

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 or 240 mg/kg/day of the 1:2 ratio (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 paediatric patients should not exceed 80 mg/kg/day. If more than 80 mg/kg/day of cefoperazone activity is necessary, additional cefoperazone should be administered separately.
Mode of administration: For intravenous infusion and intramuscular administration only.
Each vial of sulbactam/cefoperazone should be reconstituted with the appropriate amount of 5% Dextrose in water, 0.9% Sodium Chloride Injection or Sterile Water for Injections IP, then further diluted to 10 ml with the same solution, and followed by administration over 15 to 60 minutes. Lactated Ringerssolution is a suitable vehicle for intravenous infusion, but it is not, however, for initial reconstitution.

Lidocaine HCl 2% is a suitable vehicle for intramuscular administration; however, it is not for initial reconstitution.
Directions for use: Dissolve the contents of vial in 5 ml of Sterile Water for Injections IP for IM use & 10 ml for IV use and further dilute with vehicle for IV infusion. The constituted solution should be used immediately after preparation.
For intravenous injection, each vial should be reconstituted as above and administered over a minimum of 3 minutes.
For intravenous infusion, diluted solution to be administration over 15 to 60 minutes.

CONTRAINDICATIONS
Contraindicated in patients with a known allergy to penicillins, Sulbactam, Cefoperazone, or any of the cephalosporins.

SPECIAL WARNINGS & PRECAUTIONS
Cefoperazone should be cautiously administered to penicillin sensitive patients. Pseudomembranous colitis has been reported with the use of Cephalosporins and other broad spectrum antibiotics. A disulfiram-like reaction reported when alcohol was ingested within 72 hours of Cefoperazone administration. Patients should be advised not to take alcohol with Cefoperazone.

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.

USE IN SPECIAL POPULATIONS
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.
Lactation: Caution should be exercised when Sulbactam / Cefoperazone is administered to a nursing mother.
Paediatric Use: There are no significant changes in the pharmacokinetics of the components of Sulbactam / Cefoperazone, compared to adult values. The mean half-life in children has ranged from 0.91 to 1.42 hours for Sulbactam and from 1.44 to 1.88 hours for Cefoperazone. It has not been extensively studied in premature infants or neonates. Therefore, in treating premature infants and neonates potential benefits and possible risks involved should be considered before instituting therapy.
Geriatric Use : Both Sulbactam and Cefoperazone exhibited longer half-life, lower clearance and larger volumes of distribution when compared to data from normal volunteers. The pharmacokinetics of sulbactam correlated well with the degree of renal dysfunction while for Cefoperazone, there was a good correlation with the degree of hepatic dysfunction.

UNDESIRABLE 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.
Postmarketing Experience: The following additional undesirable effects have been reported:
General: Anaphylactoid reaction (including shock).
Cardiovascular: Hypotension.
Gastrointestinal: Pseudomembranous colitis.
Haematopoietic: Leucopenia.
Skin/Appendages: Pruritus, Stevens-Johnson syndrome.
Urinary: Haematuria.
Vascular: Vasculitis.

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. The fact that high cerebrospinal fluid concentrations of beta-lactam antibiotics may cause neurological effects, including seizures, should be considered. Because Cefoperazone and Sulbactam are both removed from the circulation by haemodialysis, these procedures may enhance the elimination of the drug from the body if overdosage occurs in patients with impaired renal function.

INCOMPATIBILITY
- Solutions of sulbactam/cefoperazone and aminoglycosides should not be directly mixed, since there is a physical incompatibility between them. If combination therapy with sulbactam/cefoperazone and an aminoglycoside is contemplated, this can beaccomplished by sequential intermittent intravenous infusion, provided that a separate secondary intravenous tubing is used and that the primary intravenous tubing is adequately irrigated with an approved diluent between doses.
- 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.
- Initial reconstitution with 2% lidocaine HCl solution should be avoided since this mixture has been shown to be incompatible. However, a two-step dilution processinvolving initial reconstitution in Sterile water for injection will result in a compatible mixture when further diluted with 2% lidocaine HCl solution.

STORAGE CONDITIONS
Store below 30°C. Protect from light & moisture. Do not freeze.
Keep medicine out of reach of children.

PRESENTATION
Galencef-S Forte 3gm is available in a vial and packed in mono carton, SWFI with pack Insert.

Manufactured by : Malik Lifesciences Pvt. Ltd.
(A subsidiary of **Akums Drugs & Pharmaceuticals Ltd.**)
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