Front

Cefobact™

(Cefoperazone + Sulbactam) Injection

For Intravenous &
Intramuscular Use Only

سیفوبیکٹ
انجکشن

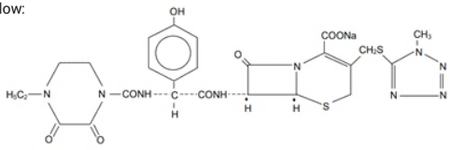
COMPOSITION:
Cefobact Injection 1 gm:
Each vial contains:
Cefoperazone (as sodium) ..... 500 mg.
Sulbactam (as sodium) ..... 500 mg.

Product Specs.: JP

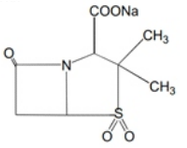
Cefobact Injection 2 gm:
Each vial contains:
Cefoperazone (as sodium) ..... 1 gm.
Sulbactam (as sodium) ..... 1 gm.

Product Specs.: JP

DESCRIPTION:
Cefoperazone, formerly known as sterile cefoperazone sodium, contains cefoperazone as cefoperazone sodium. It is a semisynthetic, broad-spectrum cephalosporin antibacterial drug. Chemically, cefoperazone sodium is sodium (6R,7R)-7-[(R)-2-(4-ethyl-2,3dioxo-1-piperazinecarboxamido)-2-(p-hydroxyphenyl)-acetamido-3-[[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate. Its molecular formula is $C_{25}H_{26}N_9NaO_8S_2$ with a molecular weight of 667.65.
The structural formula is given below:



Sulbactam sodium is a derivative of the basic penicillin nucleus. Chemically, sulbactam sodium is sodium penicillinate sulfone; sodium (2S, 5R)-3,3-dimethyl-7-oxo-4-thia1-azabicyclo [3.2.0] heptane-2-carboxylate 4,4-dioxide. Its chemical formula is $C_8H_{10}NNaO_5S$ with a molecular weight of 255.22. The structural formula is:



CLINICAL PHARMACOLOGY:
Mechanism of Action:
Cefoperazone, a third-generation cephalosporin, interferes with cell wall synthesis by binding to the penicillin-binding proteins (PBPs), thus preventing cross-linking of nascent peptidoglycan. Cefoperazone is stable to penicillinases and has a high degree of stability to many beta-lactamases produced by gram-negative bacteria.
The anti-bacterial component of sulbactam/cefoperazone combination is cefoperazone, a third-generation cephalosporin, which acts against sensitive organisms during the stage of active multiplication by inhibiting biosynthesis of cell wall mucopeptide. Sulbactam does not possess any useful antibacterial activity, except against Neisseriaceae and Acinetobacter. Sulbactam acts as a beta lactamase inhibitor, thus restoring cefoperazone activity against beta lactamase producing strains. The combination of sulbactam and cefoperazone is active against all organisms sensitive to cefoperazone.
Pharmacodynamics & Pharmacokinetics:
High serum and bile levels of Cefoperazone are attained after a single dose of the drug.
The mean serum half-life of Cefoperazone is approximately 02 hours, independent of the route of administration. Half life of Sulbactam is 01 hour. Cefoperazone is excreted mainly in the bile. Maximum bile concentrations are generally obtained between one- and three-hours following drug administration and exceed concurrent serum concentrations by up to 100 times. Reported biliary concentrations of cefoperazone range from 66 mcg/mL at 30 minutes to as high as 6000 mcg/mL at 3 hours after an intravenous bolus injection of 2 grams.
Following a single intravenous dose, the urinary recovery of Cefoperazone over a 12-hour period averages 20–30%. No significant quantity of metabolites has been found in the urine. Urinary concentrations greater than 2200 mcg/mL have been obtained following a 15-minute infusion of a 2 g dose.

MICROBIOLOGY:
Sulbactam/Cefoperazone is active in vitro against a wide variety of clinically significant organisms.
Gram-Positive Organisms:
Staphylococcus aureus (methicillin-susceptible isolates only), Staphylococcus epidermidis (methicillin-susceptible isolates only), Streptococcus agalactiae (Group B beta-hemolytic streptococci), Streptococcus pneumoniae, Streptococcus pyogenes (Group A beta-hemolytic streptococci).
Gram-Negative Organisms:
Citrobacter species, Enterobacter species, Escherichia coli, Haemophilus influenzae, Klebsiella species, Morganella morganii, Neisseria gonorrhoeae, Proteus mirabilis, Proteus vulgaris, Providencia rettgeri, Providencia stuartii, Pseudomonas species, Serratia marcescens.
Anaerobic Organisms:
Gram-positive cocci (including Peptococcus and Peptostreptococcus spp.), Clostridium species (with the exception of C. difficile), Bacteroides species (gram negative).

INDICATIONS:
Cefoperazone should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.
Cefoperazone is indicated for the treatment of the following infections when caused by susceptible organisms:
Respiratory tract infections:
Caused by S. pneumoniae, H. influenzae, S. aureus (penicillinase and non-penicillinase producing strains), S. pyogenes* (Group A beta-hemolytic streptococci), P. aeruginosa, Klebsiella pneumoniae, E. coli, Proteus mirabilis, and Enterobacter species.
Peritonitis and other intra-abdominal infections:
Caused by E. coli, P. aeruginosa, * and anaerobic gram-negative bacilli (including Bacteroides fragilis). Bacterial Septicemia caused by S. pneumoniae, S. agalactiae, * S. aureus, Pseudomonas aeruginosa, *E. coli, Klebsiella spp., *Klebsiella pneumoniae, *Proteus species* (indole-positive and indole-negative), Clostridium spp.* and anaerobic gram-positive cocci.*
Infections of the skin and skin structures:
Caused by S. aureus (penicillinase and non-penicillinase producing strains), S. pyogenes, * and P. aeruginosa.
Pelvic inflammatory disease, Endometritis, and other infections of the female genital tract:
Caused by N. gonorrhoeae, S. epidermidis, * S. agalactiae, E. coli, Clostridium spp., * Bacteroides species (including Bacteroides fragilis), and anaerobic gram-positive cocci. Cefoperazone has no activity against Chlamydia trachomatis. Therefore, when Cefoperazone is used in the treatment of patients with pelvic inflammatory disease and C. trachomatis is one of the suspected pathogens, appropriate anti-chlamydial coverage should be added.
Urinary tract infections:
Caused by Escherichia coli and Pseudomonas aeruginosa.
Enterococcal infections:
Cefoperazone should be used in enterococcal infections with care and at doses that achieve satisfactory serum levels of cefoperazone.
* Efficacy against this organism in this organ system was studied in fewer than 10 infections.
Combination therapy:
Synergy between Cefoperazone and aminoglycosides has been demonstrated with many gram-negative bacilli. However, such enhanced activity of these combinations is not predictable. If such therapy is considered, in vitro susceptibility tests should be performed to determine the activity of the drugs in combination, and renal function should be monitored carefully.

DOSAGE AND ADMINISTRATION:
The usual adult daily dose of cefoperazone alone is 2 to 4 grams per day administered in equally divided doses every 12 hours.
Daily dosage recommendations for sulbactam/cefoperazone in **adults** are as follows:

Ratio	SBT/CPZ (g)	Sulbactam Activity (g)	Cefoperazone Activity (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 cefoperazone/sulbactam 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.
Dose in renal impairment:
Dose should be adjusted in patients with 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 administered 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). In severe infections, it

may be necessary to administer additional cefoperazone. The pharmacokinetic profile of sulbactam is significantly altered by hemodialysis. The serum half-life of cefoperazone is reduced slightly during hemodialysis. Thus, dosing should be scheduled to follow a dialysis period.
Daily dosage recommendations for cefoperazone/sulbactam in **children** are as follows:

Ratio	SBT/CPZ (mg/kg/day)	Sulbactam Activity (mg/kg/day)	Cefoperazone Activity (mg/kg/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 160mg/kg/day, Doses should be administered in two to four equally divided doses or as directed by the physician.
Use in neonates: For neonates in the first week of life, 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 separately or as directed by the physician.

RECONSTITUTION:
Reconstitute vials labelled as 1 g and 2 g with 3.4 mL and 6.7 mL of compatible diluent, respectively. Appropriate diluents include sterile water for injection, 5% dextrose in water, or 0.9% NaCl. Further dilute the reconstituted solution to 20 mL using the same diluent of the initial solution or with Lactated ringer's solution.

WARNINGS & PRECAUTIONS:
Hypersensitivity: 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. Serious anaphylactic reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should be administered as indicated.
Hepatic dysfunction: Cefoperazone is extensively excreted in bile. The serum half-life of cefoperazone is usually prolonged and urinary excretion of the drug increased in patients with hepatic diseases and/or biliary obstruction. Even with severe hepatic dysfunction, therapeutic concentrations of cefoperazone are obtained in bile and only a 2 to 4 fold increase in half-life is seen. 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 patients with hepatic dysfunction and concomitant renal impairment, cefoperazone serum concentrations should be monitored and dosage adjusted as necessary. In these cases, dosage should not exceed 2 g/day of cefoperazone without close monitoring of serum concentrations.
Vitamin K deficiency: Has occurred in a few patients treated with cefoperazone. The mechanism is most probably related to the suppression of gut flora which normally synthesize this vitamin. Those at risk include patients with poor diet, malabsorption states (e.g., cystic fibrosis) and patients on prolonged intravenous alimentation regimens. Prothrombin time should be monitored in these patients, and patients receiving anticoagulant therapy, and exogenous vitamin K administered as indicated.
Overgrowth of nonsusceptible organisms may occur during prolonged use of sulbactam/cefoperazone. Patients should be observed carefully during treatment.
Sulbactam/cefoperazone: Has been effectively used in infants. 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.
Clostridium difficile associated diarrhea (CDAD): Has been reported with use of nearly all antibacterial agents, including sulbactam sodium/cefoperazone sodium, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C difficile.C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy.
CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

SPECIAL POPULATIONS:
Pregnancy:
Cefoperazone should be used during pregnancy only if clearly needed. 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 Sulbactum/Cefoperazone is administered to a nursing mother.
Nursing mothers:
Although cefoperazone passes poorly into breast milk of nursing mothers, caution should be exercised when cefoperazone is administered to a nursing woman.
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

CONTRAINDICATIONS:
Cefoperazone/sulbactam is contraindicated in patients with known allergy to penicillin, sulbactam, cefoperazone, or any of the cephalosporins.

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.
Probenecid decreases the renal tubular secretion sulbactam.
May increase INR with anticoagulants (e.g. warfarin) thereby potentiating the risk for bleeding.

ADVERSE REACTIONS:
The most frequent reported adverse effects of sulbactam/cefoperazone are diarrhea, loose stools, nausea, vomiting, hypersensitivity manifested by maculopapular, urticaria, slight decreases in neutrophils, reversible neutropenia, positive direct Coombs test, decreased hemoglobin, hematocrit, eosinophilia, thrombocytopenia, hypo-prothrombinemia, headache, fever, injection pain, chills, transient elevations of liver function tests, SGO and SGPT, alkaline phosphatase and bilirubin level and phlebitis at the infusion site. The other reported adverse effects are anaphylactoid reaction (including shock), hypotension, pseudomembranous colitis, pruritus, Stevens Johnson Syndrome, hematuria, and vasculitis.

OVERDOSAGE:
Limited information is available on the acute toxicity of cefoperazone sodium and sulbactam 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. The fact that high CSF concentrations of βlactam antibiotics may cause neurologic effects, including seizures, should be considered. Because cefoperazone and sulbactam are both removed from the circulation by hemodialysis, these procedures may enhance elimination of the drug from the body if over dosage occurs in patients with impaired renal function.

INSTRUCTIONS:
- Store in a cool and dry place, below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- Do not freeze.
- To be sold on the prescription of a registered medical practitioner only.

DIRECTIONS FOR RECONSTITUTION:
For 1 gm Injection: Add 3.4 ml sterile water in the vial for making solution.
For 2 gm Injection: Add 6.7 ml sterile water in the vial for making solution.
- Always use freshly reconstituted solution.
- Discard any remaining portion after administration.

PRESENTATION:
Cefobact Injection 1 gm : Pack of 1 gm injection 1 vial + 5 ml Solvent water for injection.
Cefobact Injection 2 gm : Pack of 2 gm injection 1 vial + 10 ml Solvent water for injection.

ہدایات:
دوا کو خشک اور ٹھنڈی جگہ، ۳۰ درجہ سینٹی گریڈ سے
کم درجہ حرارت پر رکھیں۔ گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔ منجمد ہونے سے بچائیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

دوا تیار کرنے کا طریقہ:
۱ گرام انجکشن کیلئے: محلول بنانے کیلئے جراثیم سے پاک 3.4 ملی لیٹر پانی استعمال کریں۔
۲ گرام انجکشن کیلئے: محلول بنانے کیلئے جراثیم سے پاک 6.7 ملی لیٹر پانی استعمال کریں۔
انجکشن تیار کرنے کے فوراً بعد استعمال کریں۔
استعمال کے بعد بچ جانے والا محلول ضائع کر دیں۔

Manufactured by:
Pharmasol (Pvt.) Ltd.
Plot No. 549, Sunder Industrial Estate, Lahore, Pakistan.

FOR FURTHER INFORMATION PLEASE CONTACT:

Marketed by:
CCL Pharmaceuticals (Pvt.) Ltd.
62 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.

zoom view Front

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(Cefoperazone + Sulbactam) Injection

For Intravenous &
Intramuscular Use Only

سیفوبیکٹ
انجکشن

COMPOSITION:
Cefobact Injection 1 gm:
Each vial contains:
Cefoperazone (as sodium) ..... 500 mg.
Sulbactam (as sodium) ..... 500 mg.

Product Specs.: JP

Cefobact Injection 2 gm:
Each vial contains:
Cefoperazone (as sodium) ..... 1 gm.
Sulbactam (as sodium) ..... 1 gm.

Product Specs.: JP

DESCRIPTION:
Cefoperazone, formerly known as sterile cefoperazone sodium, contains cefoperazone as cefoperazone sodium. It is a semisynthetic, broad-spectrum cephalosporin antibacterial drug. Chemically, cefoperazone sodium is sodium (6R,7R)-7-[(R)-2-(4-ethyl-2,3dioxo-1-piperazinecarboxamido)-2-(p-hydroxyphenyl)-acetamido-3-[[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate. Its molecular formula is $C_{25}H_{26}N_9NaO_8S_2$ with a molecular weight of 667.65.
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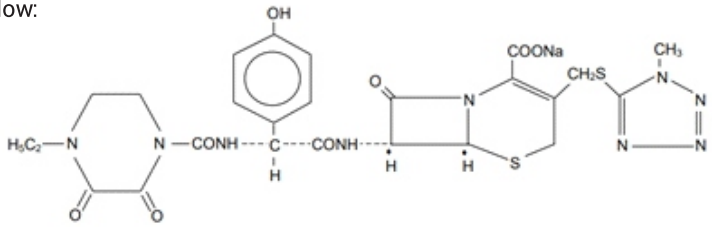

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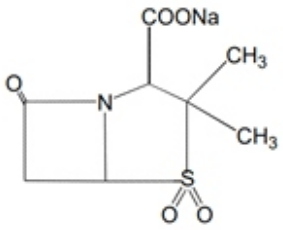

CLINICAL PHARMACOLOGY:
Mechanism of Action:
Cefoperazone, a third-generation cephalosporin, interferes with cell wall synthesis by binding to the penicillin-binding proteins (PBPs), thus preventing cross-linking of nascent peptidoglycan. Cefoperazone is stable to penicillinases and has a high degree of stability to many beta-lactamases produced by gram-negative bacteria.
The anti-bacterial component of sulbactam/cefoperazone combination is cefoperazone, a third-generation cephalosporin, which acts against sensitive organisms during the stage of active multiplication by inhibiting biosynthesis of cell wall mucopeptide. Sulbactam does not possess any useful antibacterial activity, except against Neisseriaceae and Acinetobacter. Sulbactam acts as a beta lactamase inhibitor, thus restoring cefoperazone activity against beta lactamase producing strains. The combination of sulbactam and cefoperazone is active against all organisms sensitive to cefoperazone.
Pharmacodynamics & Pharmacokinetics:
High serum and bile levels of Cefoperazone are attained after a single dose of the drug.
The mean serum half-life of Cefoperazone is approximately 02 hours, independent of the route of administration. Half life of Sulbactam is 01 hour. Cefoperazone is excreted mainly in the bile. Maximum bile concentrations are generally obtained between one- and three-hours following drug administration and exceed concurrent serum concentrations by up to 100 times. Reported biliary concentrations of cefoperazone range from 66 mcg/mL at 30 minutes to as high as 6000 mcg/mL at 3 hours after an intravenous bolus injection of 2 grams.
Following a single intravenous dose, the urinary recovery of Cefoperazone over a 12-hour period averages 20–30%. No significant quantity of metabolites has been found in the urine. Urinary concentrations greater than 2200 mcg/mL have been obtained following a 15-minute infusion of a 2 g dose.

MICROBIOLOGY:
Sulbactam/Cefoperazone is active in vitro against a wide variety of clinically significant organisms.
Gram-Positive Organisms:
Staphylococcus aureus (methicillin-susceptible isolates only), Staphylococcus epidermidis (methicillin-susceptible isolates only), Streptococcus agalactiae (Group B beta-hemolytic streptococci), Streptococcus pneumoniae, Streptococcus pyogenes (Group A beta-

hemolytic streptococci).

Gram-Negative Organisms:

Citrobacter species, Enterobacter species, Escherichia coli, Haemophilus influenzae, Klebsiella species, Morganella morganii, Neisseria gonorrhoeae, Proteus mirabilis, Proteus vulgaris, Providencia rettgeri, Providencia stuartii, Pseudomonas species, Serratia marcescens.

Anaerobic Organisms:

Gram-positive cocci (including Peptococcus and Peptostreptococcus spp.), Clostridium species (with the exception of C. difficile), Bacteroides species (gram negative).

INDICATIONS:

Cefoperazone should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.

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

Respiratory tract infections:

Caused by S. pneumoniae, H. influenzae, S. aureus (penicillinase and non-penicillinase producing strains), S. pyogenes* (Group A beta-hemolytic streptococci), P. aeruginosa, Klebsiella pneumoniae, E. coli, Proteus mirabilis, and Enterobacter species.

Peritonitis and other intra-abdominal infections:

Caused by E. coli, P. aeruginosa, * and anaerobic gram-negative bacilli (including Bacteroides fragilis). Bacterial Septicemia caused by S. pneumoniae, S. agalactiae, * S. aureus, Pseudomonas aeruginosa, *E. coli, Klebsiella spp., *Klebsiella pneumoniae, *Proteus species* (indole-positive and indole-negative), Clostridium spp.* and anaerobic gram-positive cocci.*

Infections of the skin and skin structures:

Caused by S. aureus (penicillinase and non-penicillinase producing strains), S. pyogenes, * and P. aeruginosa.

Pelvic inflammatory disease, Endometritis, and other infections of the female genital tract:

Caused by N. gonorrhoeae, S. epidermidis, * S. agalactiae, E. coli, Clostridium spp., * Bacteroides species (including Bacteroides fragilis), and anaerobic gram-positive cocci. Cefoperazone has no activity against Chlamydia trachomatis. Therefore, when Cefoperazone is used in the treatment of patients with pelvic inflammatory disease and C. trachomatis is one of the suspected pathogens, appropriate anti-chlamydial coverage should be added.

Urinary tract infections:

Caused by Escherichia coli and Pseudomonas aeruginosa.

Enterococcal infections:

Cefoperazone should be used in enterococcal infections with care and at doses that achieve satisfactory serum levels of cefoperazone.

* Efficacy against this organism in this organ system was studied in fewer than 10 infections.

Combination therapy:

Synergy between Cefoperazone and aminoglycosides has been demonstrated with many gram-negative bacilli. However, such enhanced activity of these combinations is not predictable. If such therapy is considered, in vitro susceptibility tests should be performed to determine the activity of the drugs in combination, and renal function should be monitored carefully.

DOSAGE AND ADMINISTRATION:

The usual adult daily dose of cefoperazone alone is 2 to 4 grams per day administered in equally divided doses every 12 hours.

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

Ratio	SBT/CPZ (g)	Sulbactam Activity (g)	Cefoperazone Activity (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 cefoperazone/sulbactam 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.

Dose in renal impairment:

Dose should be adjusted in patients with 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 administered 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). In severe infections, it

may be necessary to administer additional cefoperazone. The pharmacokinetic profile of sulbactam is significantly altered by hemodialysis. The serum half-life of cefoperazone is reduced slightly during hemodialysis. Thus, dosing should be scheduled to follow a dialysis period.
Daily dosage recommendations for cefoperazone/sulbactam in **children** are as follows:

Ratio	SBT/CPZ (mg/kg/day)	Sulbactam Activity (mg/kg/day)	Cefoperazone Activity (mg/kg/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 160mg/kg/day, Doses should be administered in two to four equally divided doses or as directed by the physician.
Use in neonates: For neonates in the first week of life, 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 separately or as directed by the physician.

RECONSTITUTION:
Reconstitute vials labelled as 1 g and 2 g with 3.4 mL and 6.7 mL of compatible diluent, respectively. Appropriate diluents include sterile water for injection, 5% dextrose in water, or 0.9% NaCl. Further dilute the reconstituted solution to 20 mL using the same diluent of the initial solution or with Lactated ringer's solution.

WARNINGS & PRECAUTIONS:
Hypersensitivity: 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. Serious anaphylactic reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should be administered as indicated.
Hepatic dysfunction: Cefoperazone is extensively excreted in bile. The serum half-life of cefoperazone is usually prolonged and urinary excretion of the drug increased in patients with hepatic diseases and/or biliary obstruction. Even with severe hepatic dysfunction, therapeutic concentrations of cefoperazone are obtained in bile and only a 2 to 4 fold increase in half-life is seen. 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 patients with hepatic dysfunction and concomitant renal impairment, cefoperazone serum concentrations should be monitored and dosage adjusted as necessary. In these cases, dosage should not exceed 2 g/day of cefoperazone without close monitoring of serum concentrations.
Vitamin K deficiency: Has occurred in a few patients treated with cefoperazone. The mechanism is most probably related to the suppression of gut flora which normally synthesize this vitamin. Those at risk include patients with poor diet, malabsorption states (e.g., cystic fibrosis) and patients on prolonged intravenous alimentation regimens. Prothrombin time should be monitored in these patients, and patients receiving anticoagulant therapy, and exogenous vitamin K administered as indicated.
Overgrowth of nonsusceptible organisms may occur during prolonged use of sulbactam/cefoperazone. Patients should be observed carefully during treatment.
Sulbactam/cefoperazone: Has been effectively used in infants. 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.
Clostridium difficile associated diarrhea (CDAD): Has been reported with use of nearly all antibacterial agents, including sulbactam sodium/cefoperazone sodium, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C difficile.C. difficile produces toxins A and B which contribute to the development of CDAD.
Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy.
CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

SPECIAL POPULATIONS:
Pregnancy:
Cefoperazone should be used during pregnancy only if clearly needed. 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 Sulbactum/Cefoperazone is administered to a nursing mother.
Nursing mothers:
Although cefoperazone passes poorly into breast milk of nursing mothers, caution should be exercised when cefoperazone is administered to a nursing woman.
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

CONTRAINDICATIONS:
Cefoperazone/sulbactam is contraindicated in patients with known allergy to penicillin, sulbactam, cefoperazone, or any of the cephalosporins.

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.
Probenecid decreases the renal tubular secretion sulbactam.
May increase INR with anticoagulants (e.g. warfarin) thereby potentiating the risk for bleeding.

ADVERSE REACTIONS:
The most frequent reported adverse effects of sulbactam/cefoperazone are diarrhea, loose stools, nausea, vomiting, hypersensitivity

manifested by maculopapular, urticaria, slight decreases in neutrophils, reversible neutropenia, positive direct Coombs test, decreased hemoglobin, hematocrit, eosinophilia, thrombocytopenia, hypo-prothrombinemia, headache, fever, injection pain, chills, transient elevations of liver function tests, SGO and SGPT, alkaline phosphatase and bilirubin level and phlebitis at the infusion site. The other reported adverse effects are anaphylactoid reaction (including shock), hypotension, pseudomembranous colitis, pruritus, Stevens Johnson Syndrome, hematuria, and vasculitis.

OVERDOSAGE:
Limited information is available on the acute toxicity of cefoperazone sodium and sulbactam 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. The fact that high CSF concentrations of βlactam antibiotics may cause neurologic effects, including seizures, should be considered. Because cefoperazone and sulbactam are both removed from the circulation by hemodialysis, these procedures may enhance elimination of the drug from the body if over dosage occurs in patients with impaired renal function.

INSTRUCTIONS:
- Store in a cool and dry place, below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- Do not freeze.
- To be sold on the prescription of a registered medical practitioner only.

DIRECTIONS FOR RECONSTITUTION:
For 1 gm Injection: Add 3.4 ml sterile water in the vial for making solution.
For 2 gm Injection: Add 6.7 ml sterile water in the vial for making solution.
- Always use freshly reconstituted solution.
- Discard any remaining portion after administration.

PRESENTATION:

Cefobact Injection 1 gm	:	Pack of 1 gm injection 1 vial + 5 ml Solvent water for injection.
Cefobact Injection 2 gm	:	Pack of 2 gm injection 1 vial + 10 ml Solvent water for injection.

ہدایات:

دوا کو خشک اور ٹھنڈی جگہ، ۳۰ درجہ سینٹی گریڈ سے
کم درجہ حرارت پر رکھیں۔ گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔ منجمند ہونے سے بچائیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

دوا تیار کرنے کا طریقہ:

۱ گرام انجکشن کیلئے: محلول بنانے کیلئے جراثیم سے پاک 3.4 ملی لیٹر پانی استعمال کریں۔
۲ گرام انجکشن کیلئے: محلول بنانے کیلئے جراثیم سے پاک 6.7 ملی لیٹر پانی استعمال کریں۔
انجکشن تیار کرنے کے فوراً بعد استعمال کریں۔
استعمال کے بعد بچ جانے والا محلول ضائع کر دیں۔

Manufactured by:
Pharmasol (Pvt.) Ltd.
Plot No. 549, Sunder Industrial Estate, Lahore, Pakistan.

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