1. NAME OF THE MEDICINAL PRODUCT

SULPERAZON

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sulbactam sodium/cefoperazone sodium combination is available as a dry powder for reconstitution in a 1:1 ratio in terms of free SBT/CPZ.

Sulbactam 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. It contains 92 mg sodium (4 mEq) per gram. Sulbactam is an off-white crystalline powder which is highly soluble in water. The molecular weight is 255.22.

Cefoperazone sodium is a semisynthetic broad-spectrum cephalosporin antibiotic for parenteral use only. It contains 34 mg sodium (1.5 mEq) per gram. Cefoperazone is a white crystalline powder which is freely soluble in water. The molecular weight is 667.65.

3. PHARMACEUTICAL FORM

Vials of the 1:1 product contain the equivalent of 500 mg + 500 mg and 1000 mg + 1000 mg of sulbactam and cefoperazone, respectively.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Monotherapy

Sulbactam/cefoperazone is 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
Septicemia
Meningitis
Skin and Soft Tissue Infections
Bone and Joint Infections
Pelvic Inflammatory Disease, Endometritis, Gonorrhea, 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 alone. However, sulbactam/cefoperazone may be used concomitantly with other antibiotics if such combinations are indicated. If an aminoglycoside is used (see section 6.2 **Incompatibilities** - *Aminoglycosides*), renal function should be monitored during the course of therapy (see section 4.2 **Posology and Method of Administration -** *Use in Renal Dysfunction*).

4.2 Posology and Method of Administration

Use in Adults

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 sulbactam/cefoperazone 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.

Use in Hepatic Dysfunction

See section 4.4 **Special Warnings and Precautions for Use**.

Use in Renal Dysfunction

Dosage regimens of sulbactam/cefoperazone 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.

Use in Elderly

See section 5.2 **Pharmacokinetic Properties**.

Use in Children

Daily dosage recommendations for sulbactam/cefoperazone 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 160 mg/kg/day of the 1:1 ratio. Doses should be administered in two to four equally divided doses (see section 4.4 **Special Warnings and Precautions for Use -** *Use in Infancy* and section 5.3 **Preclinical Safety Data** - *Use in Pediatrics*).

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 pediatrics should not exceed 80 mg/kg/day). For doses of sulbactam/cefoperazone requiring more than 80 mg/kg/day cefoperazone activity, additional cefoperazone should be administered (see section 4.4 **Special Warnings and Precautions for Use -** *Use in Infancy*).

Intravenous Administration

For intermittent infusion, each vial of sulbactam/cefoperazone should be reconstituted with the appropriate amount (see section 6.6 **Special Precautions for Disposal and Other Handling -** *Reconstitution*) of 5% Dextrose in Water, 0.9% Sodium Chloride Injection or Sterile Water for Injection and then diluted to 20 ml with the same solution followed by administration over 15 to 60 minutes.

Lactated Ringer's Solution is a suitable vehicle for intravenous infusion, however, not for initial reconstitution (see section 6.2 **Incompatibilities -** *Lactated Ringer's Solution* and section 6.6 **Special Precautions for Disposal and Other Handling** - *Lactated Ringer's Solution*).

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, not for initial reconstitution (see section 6.2 **Incompatibilities** - *Lidocaine* and section 6.6 **Special Precautions for Disposal and Other Handling -** *Lidocaine*).

4.3 Contraindications

Sulbactam/cefoperazone is contraindicated in patients with known hypersensitivity to any component of this product or to other drugs in the same class or in patients who have demonstrated severe hypersensitivity to beta-lactams (see section 4.4 **Special Warnings and Precautions for Use**).

4.4 Special Warnings and Precautions for Use

Hypersensitivity

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients receiving therapy with beta-lactams. Before initiating therapy with sulbactam/cefoperazone, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, carbapenems or other beta-lactam agents. If an allergic reaction occurs, sulbactam/cefoperazone must be discontinued immediately and appropriate alternative therapy instituted.

Serious anaphylactic reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should be administered as indicated (see section 4.8 **Undesirable Effects**).

Severe and occasionally fatal skin reactions such as toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), and dermatitis exfoliative have been reported in patients on sulbactam/cefoperazone therapy. If a severe skin reaction occurs sulbactam/cefoperazone should be discontinued and appropriate therapy should be initiated (see section 4.8 **Undesirable Effects**).

Use in 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.

General

Serious haemorrhage cases, including fatalities, have been reported with sulbactam/cefoperazone. As with other antibiotics, Vitamin K deficiency resulting in coagulopathy has occurred in patients treated with sulbactam/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. Discontinue sulbactam/cefoperazone if there is persistent bleeding and no alternative explanations are identified.

As with other antibiotics, overgrowth of non-susceptible organisms may occur during prolonged use of sulbactam/cefoperazone. Patients should be observed carefully during treatment. As with any potent systemic agent, it is advisable to check periodically for organ system dysfunction during extended therapy; this includes renal, hepatic, and hematopoietic systems. This is particularly important in neonates, especially when premature, and other infants.

Clostridioides 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.

Encephalopathy (with or without seizures) has been reported with the use of cefoperazone. Most cases occurred in patients with renal impairment. If encephalopathy occurs, discontinuation of cefoperazone should be considered and appropriate supportive measures should be taken.

Use in Infancy

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 (see section 5.3 **Preclinical Safety Data** - *Use in Pediatrics*).

Cefoperazone does not displace bilirubin from plasma protein binding sites.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Alcohol

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.

Drug Laboratory Test Interactions

A false-positive reaction for glucose in the urine may occur with Benedict's or Fehling's solution.

4.6 Fertility, Pregnancy and Lactation

Usage during Pregnancy

Reproduction studies have been performed in rats at doses up to 10 times the human dose and have revealed no evidence of impaired fertility and no teratological findings. Sulbactam and cefoperazone cross the placental barrier. There are, however, 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.

Usage in Nursing Mothers

Only small quantities of sulbactam and cefoperazone are excreted in human milk. Although both drugs

pass poorly into breast milk of nursing mothers, caution should be exercised when sulbactam/cefoperazone is administered to a nursing mother.

4.7 Effects on Ability to Drive and Use Machines

Clinical experience with sulbactam/cefoperazone indicates that it is unlikely to impair a patient's ability to drive or use machinery.

4.8 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 following ADRs were observed in clinical trials (comparative and non-comparative studies) and in the post-marketing.

All ADRs listed in the label are presented by MedDRA SOC and are presented in the order of clinical importance.

System Organ Class	Very Common ≥1/10	Common ≥1/100 to <1/10	Uncommon ≥1/1000 to <1/100	Frequency Not Known (cannot be estimated from the available data)
Blood and lymphatic system disorders	Neutropenia†, Leukopenia†, Coombs direct test positive†, Haemoglobin decreased†, Haematocrit decreased†, Thrombocytopenia†	Coagulopathy*, Eosinophilia†		Hypoprothrombinaemia*
Immune system disorders				Anaphylactic shock*§, Anaphylactic reaction*§, Anaphylactoid reaction§, including shock* Acute coronary syndrome accompanying allergic reaction*, Hypersensitivity*§
Nervous system disorders			Headache	Encephalopathy*,**
Vascular disorders				Haemorrhage*§, Vasculitis*, Hypotension*
Gastrointestinal disorders		Diarrhoea, Nausea, Vomiting		Pseudomembranous colitis*
Hepatobiliary disorders	Alanine aminotransferase increased†, Aspartate aminotransferase increased†, Blood alkaline	Blood bilirubin increased†		Jaundice*

System Organ Class	Very Common ≥1/10	Common ≥1/100 to <1/10	Uncommon ≥1/1000 to <1/100	Frequency Not Known (cannot be estimated from the available data)
	phosphatase increased†			
Skin and subcutaneous tissue disorders			Pruritus, Urticaria	Toxic epidermal necrolysis*§, Stevens Johnson syndrome*§, Dermatitis exfoliative*§, Rash maculopapular*
Renal and urinary disorders				Haematuria*
General disorders and administration site conditions			Infusion site phlebitis, Injection site pain, Pyrexia, Chills	

*ADR identified post-marketing
**With or without seizures.
†: In the calculation for laboratory abnormality ADR frequencies, all available laboratory values, including those of subjects with baseline abnormalities, were included. This conservative approach was taken because the raw data did not allow distinction between the subset of subjects with baseline abnormalities who had treatment-emergent significant laboratory changes from those subjects with baseline abnormalities who did not have treatment-emergent significant laboratory changes.
For leucocytes, neutrophils, platelets, haemoglobin and haematocrit, only abnormalities are reported in studies. Increases and decreases are not differentiated.
§: Fatalities have been reported.

4.9 Overdose

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 CSF concentrations of β-lactam 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 overdosage occurs in patients with impaired renal function.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

The anti-bacterial component of sulbactam/cefoperazone 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*. 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.

The potential for sulbactam's 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 sulbactam and cefoperazone is active against all organisms sensitive to cefoperazone. In addition it demonstrates synergistic activity (up to four-fold reduction in minimum inhibitory concentrations for the combination versus those for each component) in a variety of organisms, most markedly the following:

Haemophilus influenzae
Bacteroides species
Staphylococcus species
Acinetobacter calcoaceticus
Enterobacter aerogenes
Escherichia coli
Proteus mirabilis
Klebsiella pneumoniae
Morganella morganii
Citrobacter freundii
Enterobacter cloacae
Citrobacter diversus

Sulbactam/cefoperazone is active *in vitro* against a wide variety of clinically significant organisms:

Gram-Positive Organisms:

Staphylococcus aureus, penicillinase and non-penicillinase-producing strains
Staphylococcus epidermidis
Streptococcus pneumoniae (formerly *Diplococcus pneumoniae*)
Streptococcus pyogenes (Group A beta-hemolytic streptococci)
Streptococcus agalactiae (Group B beta-hemolytic streptococci)
Most other strains of beta-hemolytic streptococci
Many strains of *Streptococcus faecalis* (enterococcus)

Gram-Negative Organisms:

Escherichia coli
Klebsiella species
Enterobacter species
Citrobacter species
Haemophilus influenzae
Proteus mirabilis
Proteus vulgaris
Morganella morganii (formerly *Proteus morganii*)
Providencia rettgeri (formerly *Proteus rettgeri*)
Providencia species
Serratia species (including *S. marcescens*)
Salmonella and *Shigella* species
Pseudomonas aeruginosa and some other *Pseudomona*s species
Acinetobacter calcoaceticus

Neisseria gonorrhoeae
Neisseria meningitidis
Bordetella pertussis
Yersinia enterocolitica

Anaerobic Organisms:

Gram-negative bacilli (including *Bacteroides fragilis*, other *Bacteroides* species, and *Fusobacterium* species)

Gram-positive and gram-negative cocci (including *Peptococcus*, *Peptostreptococcus* and *Veillonella* species)

Gram-positive bacilli (including *Clostridioides*, *Eubacterium* and *Lactobacillus* species)

The following susceptibility ranges have been established for sulbactam/cefoperazone:

	Minimal inhibitory concentration (MIC), (mcg/ml-expressed as cefoperazone concentration)
Susceptible	≤16
Intermediate	17-63
Resistant	≥64

	Susceptibility Disc Zone Size, mm (Kirby-Bauer)
Susceptible	≥21
Intermediate	16 - 20
Resistant	≤15

For MIC determinations, serial dilutions of sulbactam/cefoperazone in a 1:1 sulbactam/cefoperazone ratio may be used with a broth or agar dilution method. Use of a susceptibility test disc containing 30 mcg of sulbactam and 75 mcg of cefoperazone is recommended. A report from the laboratory of "susceptible" indicates that the infecting organism is likely to respond to sulbactam/cefoperazone therapy, and a report of "Resistant" indicates that the organism is not likely to respond. A report of "Intermediate" suggests that the organism would be susceptible to sulbactam/cefoperazone if a higher dosage is used or if the infection is confined to tissues or fluids where high antibiotic levels are attained.

The following quality control limits are recommended for 30 mcg/75 mcg sulbactam/cefoperazone susceptibility discs:

CONTROL STRAIN	ZONE SIZE mm
Acinetobacter spp. ATCC 43498	26 - 32

Pseudomonas aeruginosa ATCC 27853	22 - 28
Escherichia coli ATCC 25922	27 - 33
Staphylococcus aureus ATCC 25923	23 - 30

5.2 Pharmacokinetic Properties

Approximately 84% of the sulbactam dose and 25% of the cefoperazone dose administered with sulbactam/cefoperazone is excreted by the kidney. 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 the agents when given alone.

Mean peak sulbactam and cefoperazone concentrations after the administration of 2 grams of sulbactam/cefoperazone (1 g sulbactam, 1 g of cefoperazone) intravenously over 5 minutes were 130.2 and 236.8 mcg/ml, respectively. This reflects the larger volume of distribution for sulbactam (Vd = 18.0-27.6 L) compared to cefoperazone (Vd = 10.2-11.3 L).

Both sulbactam and cefoperazone distribute well into a variety of tissues and fluids including bile, gall bladder, skin, appendix, fallopian tubes, ovary, uterus, and others.

There is no evidence of any pharmacokinetic drug interaction between sulbactam and cefoperazone when administered together in the form of sulbactam/cefoperazone.

After multiple dosing no significant changes in the pharmacokinetics of either component of sulbactam/cefoperazone have been reported and no accumulation has been observed when administered every 8 to 12 hours.

Use in Hepatic Dysfunction

See section 4.4 **Special Warnings and Precautions for Use**.

Use in Renal Dysfunction

In patients with different degrees of renal function administered sulbactam/cefoperazone, the total body clearance of sulbactam was highly correlated with estimated creatinine clearance. Patients who are functionally anephric showed a significantly longer half-life of sulbactam (mean 6.9 and 9.7 hours in separate studies). Hemodialysis significantly altered the half-life, total body clearance, and volume of distribution of sulbactam. No significant differences have been observed in the pharmacokinetics of cefoperazone in renal failure patients.

Use in Elderly

The pharmacokinetics of sulbactam/cefoperazone have been studied in elderly individuals with renal insufficiency and compromised hepatic function. 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.

Use in Children

Studies conducted in pediatrics have shown 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.

5.3 Preclinical Safety Data

Use in Pediatrics

Cefoperazone had adverse effects on the testes of prepubertal rats at all doses tested. Subcutaneous administration of 1,000 mg/kg per day (approximately 16 times the average adult human dose) resulted in reduced testicular weight, arrested spermatogenesis, reduced germinal cell population and vacuolation of Sertoli cell cytoplasm. The severity of lesions was dose dependent in the 100 to 1,000 mg/kg per day range; the low dose caused a minor decrease in spermatocytes. This effect has not been observed in adult rats. Histologically, the lesions were reversible at all but the highest dosage levels. However, these studies did not evaluate subsequent development of reproductive function in the rats. The relationship of these findings to humans is unknown.

When sulbactam/cefoperazone (1:1) was given subcutaneously to neonatal rats for 1 month reduced testicular weights and immature tubules were seen in groups given 300 + 300 mg/kg/day. Because there is a great individual variation in the degree of testicular maturation in rat pups and because immature testes were found in controls any relation to study drug is uncertain. No such findings were seen in infant dogs at doses over 10 times the average adult dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

None

6.2 Incompatibilities

Aminoglycosides

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 (see section 4.1 **Therapeutic Indications** - *Combination Therapy*) this can be accomplished by sequential intermittent intravenous infusion provided that separate secondary intravenous tubing is used, and that the primary intravenous tubing is adequately irrigated with an approved diluent between doses. It is also suggested that doses of sulbactam/cefoperazone be administered throughout the day at times as far removed from administration of the aminoglycoside as possible.

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 water for injection will result in a compatible mixture when further diluted with Lactated Ringer's

Solution (see section 6.6 **Special Precautions for Disposal and Other Handling** - *Lactated Ringer's Solution*).

Lidocaine

Initial reconstitution with 2% lidocaine HCl solution should be avoided since this mixture has been shown to be incompatible. However, a two step dilution process involving initial reconstitution in water for injection will result in a compatible mixture when further diluted with 2% lidocaine HCl solution (see section 6.6 **Special Precautions for Disposal and Other Handling** - *Lidocaine*).

6.3 Shelf-life

24 months (dry powder)
1 day (reconstituted suspension at room temperature).

6.4 Special Precautions for Storage

Store below 30°C and protected from light.

6.5 Nature and Contents of Container

Sulbactam/cefoperazone is available in 1.0 g and 2.0 g strength vials.

Some product strengths or pack sizes may not be available in your country.

6.6 Special Precautions for Disposal and Other Handling

Reconstitution

Total Dosage (g)	Equivalent Dosage of sulb. + cefoperazone (g)	Volume of Diluent	Maximum Final Conc. (mg/ml)
1.0	0.5 + 0.5	3.4	125 + 125
2.0	1.0 + 1.0	6.7	125 + 125

Sulbactam/cefoperazone has been shown to be compatible with these diluents: water for injection, 5% dextrose, normal saline, 5% dextrose in 0.225% saline, and 5% dextrose in normal saline. Cefoperazone is compatible at concentrations ranging from 10-250 mg/ml of diluent. Sulbactam is compatible at concentrations ranging from 5-125 mg/ml of diluent.

Lactated Ringer's Solution

Sterile Water for Injection should be used for reconstitution (see section 6.2 **Incompatibilities** - *Lactated Ringer's Solution*). A two-step dilution is required using Sterile Water for Injection (shown in table above) further diluted with Lactated Ringer's Solution to a sulbactam concentration of 5 mg/ml (use 2 ml initial dilution in 50 ml or 4 ml initial dilution in 100 ml Lactated Ringer's Solution).

Lidocaine

Sterile Water for Injection should be used for reconstitution (see section 6.2 **Incompatibilities** -

Lidocaine). For a concentration of cefoperazone of 250 mg/ml or larger, a two-step dilution is required using Sterile Water for Injection (shown in table above) further diluted with 2% lidocaine to yield solutions containing up to 125 mg cefoperazone and 125 mg sulbactam per ml in approximately a 0.5% lidocaine HCl solution.

7. MANUFACTURER

Qilu Antibiotics Pharmaceutical Co., Ltd.,
Shandong Province, China.

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