SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE PRODUCT

2Sum® (Cefoperazone Sodium + Sulbactam Sodium) 500mg Injection

2Sum® (Cefoperazone Sodium + Sulbactam Sodium) 1g Injection

2Sum® (Cefoperazone Sodium + Sulbactam Sodium) 2g Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2Sum® 500mg Injection
Each vial contains:
Sterile Cefoperazone Sodium MS equivalent to Cefoperazone.....250mg
Sterile Sulbactam Sodium MS equivalent to Sulbactam.....250mg

2Sum® 1g Injection
Each vial contains:
Sterile Cefoperazone Sodium MS equivalent to Cefoperazone.....500mg
Sterile Sulbactam Sodium MS equivalent to Sulbactam.....500mg

2Sum® 2g Injection
Each vial contains:
Sterile Cefoperazone Sodium MS equivalent to Cefoperazone.....1g
Sterile Sulbactam Sodium MS equivalent to Sulbactam.....1g

3. PHARMACEUTICAL FORM

Injection

Appearance:

2Sum® 500mg Injection: White to off-white powder free from visible particles.

2Sum® 1g Injection: White to off-white powder free from visible particles.

2Sum® 2g Injection: White to off-white powder free from visible particles.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS:

Mono-therapy: 2Sum® is indicated for the treatment of the following infections when caused by susceptible organisms:
● Respiratory Tract Infections ● Urinary Tract Infections (Upper and Lower) ● Intra-abdominal Infections ● Septicemia ● Meningitis ● Skin and Soft Tissue Infections ● Bone and Joint Infections ● Endometritis ● Other Infections of the Genital Tract (Bartholin's gland inflammation, intrauterine infection, uterine adnexitis, uterine phlegmonitis) ● Sepsis ● Infective endocarditis ● Secondary infections from trauma ● Burns, surgical wounds ● Pneumonia ● Secondary infections from chronic respiratory lesions ● Cholecystitis ● Cholangitis ● Liver abscess
Concomitant Use: Because of the broad-spectrum of activity of cefoperazone/sulbactam, 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, renal function should be monitored during the course of therapy.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION:

2Sum® (cefoperazone sodium/sulbactam sodium combination) is available in bottles for parenteral use only.
Posology:
Use in Adults: The usual adult dose of cefoperazone/sulbactam is 2 to 4g per day (i.e. 1 to 2g per day cefoperazone activity) given intravenously or intramuscularly in equally divided doses every 12 hours.

Ratio	SBT/CPZ (g)	Sulbactam Activity (g)	Cefoperazone Activity (g)
1:1	2.0 - 4.0	1.0 - 2.0	1.0 - 2.0

The recommended maximum daily dosage of sulbactam is 4g (i.e., 8g of cefoperazone/sulbactam). In febrile neutropenia, total daily dose can be administered twice or thrice a day in equally divided doses.
Use in Hepatic Dysfunction: See Special Warnings and Precautions for Use.
Use in Renal Dysfunction: Dosage regimens of cefoperazone/sulbactam should be adjusted in patients with marked decrease in renal function (creatinine clearance of less than 30ml/min) to compensate for the reduced clearance of sulbactam. Patients with creatinine clearances between 15 and 30ml/min should receive a maximum of 1g of sulbactam administered every 12 hours (maximum daily dosage of 2g sulbactam), while patients with creatinine clearances of less than 15ml/min should receive a maximum of 500mg of sulbactam every 12 hours (maximum daily dosage of 1g sulbactam). In severe infections it may be necessary to administer additional cefoperazone separately. 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.
Use in Elderly: See Pharmacokinetic Properties.
Paediatric Population: The usual dosage of cefoperazone/sulbactam in children is 40 to 80mg/kg/day (i.e. 20-40mg/kg/day cefoperazone) in 2 to 4 equally divided doses.

Ratio	SBT/CPZ (mg/kg/day)	Sulbactam Activity mg/kg/day	Cefoperazone Activity mg/kg/day
1:1	40 - 80	20 - 40	20 -40

In serious or refractory infections, these dosages may be increased up to 160mg/kg/day (80mg/kg/day of cefoperazone) of the 1:1 ratio. Doses should be administered in 2 to 4 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 80mg/kg/day.
Method of Administration:
Intravenous Administration: For intermittent infusion, each vial of cefoperazone/sulbactam should be reconstituted with the appropriate amount of 5% Dextrose in Water, 0.9% Sodium Chloride Injection or Sterile Water for Injection and then diluted to 20ml 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. For intravenous injection, each vial should be reconstituted as above and administered over a minimum of 3 minutes.
Intramuscular Administration: Lidocaine hydrochloride 2% is a suitable vehicle for intramuscular administration, however, not for initial reconstitution.

4.3. CONTRAINDICATIONS:

Hypersensitivity to the active substances (cefoperazone, sulbactam), to beta-lactams or to any of the excipients.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

Hypersensitivity: Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients receiving beta-lactam or cephalosporin therapy, including cefoperazone/sulbactam. These reactions are more apt to occur in individuals with a history of hypersensitivity reactions to multiple allergens. Before therapy with cefoperazone/sulbactam is instituted, careful inquiry should be made to determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins or other drugs. Antibiotics should be administered with caution to any patient who has demonstrated some form of allergy, particularly to drugs. 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. 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 cefoperazone/sulbactam therapy. If a severe skin reaction occurs cefoperazone/sulbactam should be discontinued and appropriate therapy should be initiated.
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 2g/day of cefoperazone without close monitoring of serum concentrations.
General: Haemorrhage cases, sometimes fatal including fatalities, have been reported with the use of cefoperazone/sulbactam. As with other antibiotics, a vitamin K deficiency has occurred in patients treated with cefoperazone/sulbactam which has generated coagulopathy. The mechanism is most likely connected with the suppression of the intestinal bacterial flora that normally synthesizes this vitamin. Those at risk include patients with poor diet, malabsorption conditions and patients, and in patients receiving oral anticoagulants, prothrombin time (or INR) on prolonged intravenous alimentation regimens. In these patients should be monitored (for signs of bleeding, thrombocytopenia and hypoprothrombinemia) and exogenous vitamin K should be given as indicated. Discontinue cefoperazone/sulbactam in case of persistent bleeding and no alternative explanation is identified. As with other antibiotics, overgrowth of non-susceptible organisms may occur during prolonged use of cefoperazone/sulbactam. 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 haematopoietic systems. This is particularly important in neonates, especially when premature, and other infants. *Clostridium difficile* associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including cefoperazone sodium/sulbactam sodium, and may range in severity from mild diarrhoea 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 diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.
Paediatric population: Cefoperazone/sulbactam 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. In neonates with kernicterus, cefoperazone does not displace bilirubin from plasma protein binding sites.

Central Nervous System: High concentrations of β-Lactam antibiotics in the cerebrospinal fluid may cause neurological side effects, including seizures and convulsions, should be considered.

4.5. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORM OF INTERACTIONS:
Combination Therapy: Because of the broad spectrum of activity of cefoperazone/sulbactam, many infections can be treated. However, cefoperazone/sulbactam may be used together with other antibiotics. If an aminoglycoside is used, renal function should be monitored during the course of therapy.
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:
Fertility: 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.
Pregnancy: 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, cefoperazone/sulbactam should be used during pregnancy only if clearly needed. It should be administered to pregnant women or women who may become pregnant only if the therapeutic benefits are judged to outweigh the risks.
Breast-feeding: 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 cefoperazone/sulbactam indicates that it is unlikely to impair a patient's ability to drive or use machinery.

4.8. UNDESIRABLE EFFECTS:
Cefoperazone/sulbactam is generally well tolerated. The majority of adverse events are of mild or moderate severity and are tolerated with continued treatment. The following undesirable effects have been observed and reported during treatment with sulbactam/cefoperazone with the following frequencies: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).
Blood and lymphatic system disorders: ***Very Common:*** Neutropenia, leukopenia, Coombs direct test positive, haemoglobin decreased, haematocrit decreased, thrombocytopenia. ***Common:*** Coagulopathy, eosinophilia. ***Uncommon:*** Anemia. ***Not known:*** Hypoprothrombinaemia.
Immune system disorders: ***Not known:*** Anaphylactic shock, anaphylactic reaction, anaphylactoid reaction including shock, hypersensitivity.
Nervous system disorders: ***Uncommon:*** Headache. ***Not known:*** Convulsions, seizures.
Vascular disorders: ***Not known:*** Haemorrhage (including fatal), vasculitis, hypotension.
Gastrointestinal disorders: ***Common:*** Vomiting, diarrhoea, nausea, loose stools. ***Not known:*** Pseudomembranous colitis.
Hepatobiliary disorders: ***Very common:*** Alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased. ***Common:*** Blood bilirubin increased. ***Not known:*** Jaundice.
Skin and subcutaneous tissues disorders: ***Uncommon:*** Pruritus, urticaria. ***Not known:*** Toxic epidermal necrolysis, Stevens-Johnson syndrome, dermatitis exfoliative, maculopapular rash.
Renal and urinary disorders: ***Not known:*** Haematuria.
General disorders and administration site conditions: ***Uncommon:*** Infusion site phlebitis, injection site pain, pyrexia, chills.
Bacterial replacement: ***Uncommon:*** Stomatitis, candida.
Others: ***Not known:*** Vitamin K deficiency condition (low proton anemia, bleeding tendency), vitamin B group deficiency symptoms (glossitis, stomatitis, loss of apetite, neuritis, etc), low blood pressure, vasculitis.

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 beta-lactam antibiotics may cause neurologic effects, including seizures, should be considered. Because cefoperazone and sulbactam are both removed from the circulation by haemodialysis, 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:
Pharmacotherapeutic group: Antibacterial for systemic use, combination of third-generation cephalosporin and beta-lactamase inhibitor. **ATC Code:** J01DA.
2Sum® is a combination of cefoperazone sodium/sulbactam sodium. Sulbactam sodium is a derivative of the basic penicillin nucleus. It is an irreversible beta-lactamase inhibitor for parenteral use only. Chemically it is a sodium penicillinate sulfone. It contains 92mg sodium (4mEq) 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 third-generation semisynthetic broad-spectrum cephalosporin antibiotic for parenteral use only. It contains 34mg sodium (1.5mEq) per gram. Cefoperazone is a white crystalline powder which is freely soluble in water. The molecular weight is 667.65.
Mechanism of action: The anti-bacterial component of cefoperazone/sulbactam 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 organism's sensitive to cefoperazone. In addition, it demonstrates synergistic activity (up to 4-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-haemolytic streptococci) ● *Streptococcus agalactiae* (Group B beta-haemolytic streptococci) ● Most other strains of beta-haemolytic 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 *Pseudomonas* 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 *Clostridium*, *Eubacterium* and *Lactobacillus* species). The following susceptibility ranges have been established for cefoperazone/sulbactam:

Minimal inhibitory concentration (MIC) mcg/ml expressed as cefoperazone concentrations	
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 cefoperazone/sulbactam in a 1:1 cefoperazone/sulbactam ratio may be used with a broth or agar dilution method. Use of a susceptibility test disc containing 30mcg of sulbactam and 75mcg of cefoperazone is recommended. A report from the laboratory of "susceptible" indicates that the infecting organism is likely to respond to cefoperazone/sulbactam 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 cefoperazone/sulbactam 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 30mcg/75mcg sulbactam/cefoperazone susceptibility discs:

CONTROL STRAIN	ZONE SIZE (mm)
Acinetobacter spp., ATCC 43498	26-32
Pseudomonas aeuriginosa, ATCC 27853	22-28
Escherichia coli, ATCC 25922	27-33
Staphylococcus aureus, ATCC 25923	23-30

SUMMARY OF PRODUCT CHARACTERISTICS

5.2. PHARMACOKINETICS:
Distribution: Mean peak sulbactam and cefoperazone concentrations after the administration of 2g (1:1 ratio) of cefoperazone/sulbactam (1g cefoperazone + 1g of sulbactam) intravenously over 5 minutes to healthy volunteers were 130 and 236.8mcg/ml respectively following a single dose. This reflects the larger volume of distribution for sulbactam (V_d = 18.0-27.6L) compared to cefoperazone (V_d = 10.2-11.3L).
Elimination: Approximately 84% of the sulbactam dose and 25% of the cefoperazone dose administered with cefoperazone/sulbactam is excreted by the kidney. Most of the remaining dose of cefoperazone is excreted in the bile. After cefoperazone/sulbactam 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. 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 Special Warnings and Precautions for Use.
Use in Renal Dysfunction: In patients with different degrees of renal function who were administered cefoperazone/sulbactam, 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). Haemodialysis 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 cefoperazone/sulbactam 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.
Paediatric Population: Studies conducted in paediatrics 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. Both sulbactam and cefoperazone distribute well in 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 form of 2Sum®, Cefoperazone does not displace bilirubin from plasma protein binding sites.

5.3. PRE-CLINICAL SAFETY DATA:
The pharmacotoxicity studies showed that cefoperazone/sulbactam do not increase the toxicity of the other component. The two components have been used for a long time in the clinical practice and extensive studies were conducted in the past to evaluate the pharmacotoxicology of both drugs. However, pharmacotoxicology studies either with single and repeated administrations on various animal species have shown that cefoperazone/sulbactam is well tolerated. LD_{50} after intravenous administration in male and female rats is approximately 9300mg/Kg and 8200mg/kg, respectively, while following intraperitoneal administration it is >6000mg/kg in both male and female rats. DL_{50} after intravenous administration in male and female mice is about 6900mg/kg and 7400mg/kg, respectively, while after intraperitoneal administration it is >6000mg/kg both in male and female mice. DL_{50} after intravenous administration in beagle female dogs is 2000mg/kg. Cefoperazone had adverse effects on the testes of prepubertal rats at all doses tested. Subcutaneous administration of 1,000mg/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 1,000mg/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 cefoperazone/sulbactam (1:1) was given subcutaneously to neonatal rats for 1 month reduced testicular weights and immature tubules were seen in groups given 300+300mg/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:
Not applicable

6.2. INCOMPATIBILITIES:
Solutions of cefoperazone/sulbactam and aminoglycosides should not be directly mixed, since there is a physical incompatibility between them. If combination therapy with cefoperazone/sulbactam and an aminoglycoside is contemplated 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. 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. Initial reconstitution with lidocaine hydrochloride 2% 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 lidocaine hydrochloride 2% solution.

6.3. SHELF LIFE:
Unopened vial: See expiry on pack.
Reconstituted solution: Reconstituted solutions are stable for 7 days at 2 - 8°C and for 24 hours at 8 - 25°C.

6.4. SPECIAL PRECAUTIONS FOR STORAGE:
Do not store over 30°C, and protect from heat, light and moisture. Improper storage may deteriorate the medicine.
Keep out of reach of children.

6.5. NATURE AND CONTENTS OF CONTAINER:
2Sum® **500mg Injection:** ***Powder for Injection:*** Clear glass vial (USP Type-III) with bromobutyl rubber stopper, sealed with flip off seal. ***WFI:*** Clear 2ml glass ampoule (USP Type-I), pack size is 1 vial and 1 ampoule.
2Sum® **1g Injection:** ***Powder for Injection:*** Clear glass vial (USP Type-III) with bromobutyl rubber stopper, sealed with flip off seal. ***WFI:*** Clear 4ml glass ampoule (USP Type-I), pack size is 1 vial and 1 ampoule.
2Sum® **2g Injection:** Clear glass vial (USP Type-III) with bromobutyl rubber stopper, sealed with flip off seal. ***WFI:*** Clear 10ml glass ampoule (USP Type-I), pack size is 1 vial and 1 ampoule.

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING:
Direction for Reconstitution:
For 2Sum® 500mg Injection: Dissolve vial content by vigorous shaking using 1.7ml Water for Injection provided with the pack.
For 2Sum® 1g Injection: Dissolve vial content by vigorous shaking using 3.4ml Water for Injection provided with the pack.
For 2Sum® 2g Injection: Dissolve vial content by vigorous shaking using 6.7ml Water for Injection provided with the pack.
Cefoperazone/sulbactam 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 to 250mg/ml of diluent. Sulbactam is compatible at concentrations ranging from 5 to 125mg/ml of diluent. For single use only, discard unused portion. Any unused product or waste material should be disposed in accordance with local requirements.

6.7. DRUG PRODUCT SPECIFICATION:
Mfr. Specs.

7. MARKETING AUTHORISATION HOLDER

Manufactured by:
Wealthtek (Pvt.) Limited
Plot No.14, Sector 19, Korangi Industrial Area
Karachi - Pakistan

Associate of:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, S.I.T.E., Karachi-Pakistan
www.samipharmapk.com

8. MARKETING AUTHORISATION NUMBER(S)

2Sum® **500mg Injection:** 079941
2Sum® **1g Injection:** 047002
2Sum® **2g Injection:** 047003

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

2Sum® **500mg Injection:** 9th April, 2015
2Sum® **1g Injection:** 4th September, 2007
2Sum® **2g Injection:** 4th September, 2007

10. DATE OF REVISION OF THE TEXT

ٹوسم® انجکشن
(سلبیکٹم سوڈیم + سیفوپیرازون سوڈیم)
برائے عضلاتی / وریدی استعمال

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔
صرف ایک مرتبہ استعمال کے لئے ہے غیر استعمال شدہ دوا کو ضائع کر دیں۔
بچوں کی پہنچ سے دور رکھیں۔
دوا کو ۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں،
گرمی، روشنی اور نمی سے محفوظ رکھیں ورنہ دوا خراب ہو جائیگی۔