1.3.1 Summary of product characteristics (SmPC)

Summary of products characteristics (SmPC) of Sulbacin 0.75 (Ampicillin and Sulbactam For Injection USP) is enclosed overleaf.

SUMMARY OF PRODUCTS CHARACTERISTICS

SULBACIN 0.75
(Ampicillin and Sulbactam For Injection USP)

1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

1. Name of the Medicinal Product

1.1 Product name : SULBACIN 0.75

1.2 Strength : Ampicillin and Sulbactam For Injection USP

1.3 Pharmaceutical Dosage form : Powder For Injection

2.Label Claim:

Each vial contains:
Ampicillin Sodium USP
equivalent to anhydrous Ampicillin….0.50g
Sulbactam Sodium USP
Equivalent to anhydrous Sulbactam…0.25g

SR. NO.	INGREDIENT	QTY/DOSAGE (gm)	FUNCTION	REFERENCE TO STANDARDS
1.	Ampicillin Sodium Sterile	0.50	Active	USP
2.	Sulbactam Sodium Sterile	0.25	Active	USP

3. Pharmaceutical Form

White to almost white powder aseptically filled in 10 ml USP type-I vial, closed by grey butyl rubber stopper and sealed by burgundy aluminium flip off seal.

4.1 Therapeutic indications :

Combinations of penicillins, including Beta-Lactamase inhibitors.

Sulbactam/Ampicillin is indicated in the treatment of

- Surgical prophylaxis
- Intra-abdominal infections.
- ENT infections.
- Obstetrics and Gynaecological infections.
- Bone and joint infections
- Urinary tract infections
- Respiratory tract infections

- Gonorrhoea.
- Skin and soft tissue infections.

While SULBACIN is indicated for the conditions listed above, infections caused by Ampicillin-susceptible organisms are also amenable to treatment with SULBACIN due to its Ampicillin content. Therefore, polymicrobial infections caused by Ampicillin-susceptible organisms and beta-lactamase producing organisms susceptible to SULBACIN does not require the addition of another antibiotic. Therapy may be instituted prior to obtaining bacteriological and susceptibility study results, when there is reason to believe that the infection may involve any of the beta-lactamase producing organisms listed above in the indicated organ systems. Once the results are known, therapy may be appropriately adjusted.

4.2 Posology and method of administration:

SULBACIN may be administered by either IV or the IM routes. For IV administration, the dose can be given by slow intravenous injection dissolved in 5 ml of Sterile Water for Injection I.P. over atleast 10 - 15 minutes or can also be delivered, in greater dilution with 50-100 ml of a compatible diluent as an intravenous infusion over 15-30 minutes.

SULBACIN may be administered by deep intramuscular injection (See preparation for intramuscular injection). The recommended daily dose of SULBACIN is 1 vial 6-8 hourly. The total daily dose of Sulbactam should not exceed 4 g/day. The duration of treatment depends upon the severity of infection. For antibioprophylaxis in elective surgery a different dosage regimen may be required.

4.3 Contraindications

The use of SULBACIN is contraindicated in patients with a history of hypersensitivity to any of the penicillins

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4.4 Special warning and precautions for use

Warnings

Serious and occasionally anaphylactic reactions have been reported in patients on penicillin therapy. These reactions occur in individuals with a history of penicillin hypersensitivity and/or hypersensitivity reactions to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with Cephalosporin. Before therapy with a penicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillin, cephalosporin and other allergens. If an allergic reaction occurs, SULBACIN should be discontinued and the appropriate resuscitation measures instituted. Serious anaphylactoid reactions require immediate emergency treatment with Epinephrine, Oxygen, Intravenous steroids, and air way management, including intubation should also be used as indicated.

Precautions

Ampicillin class of antibiotics should not be administered to patients with infectious mononucleosis. In patients treated with SULBACIN the possibility of super-infections with mycotic or bacterial pathogens should be kept in mind as with other beta-lactam antibiotics during therapy. If super-infections occur, the drug should be discontinued and/or appropriate therapy instituted.

4.5 Interaction with other medicinal products and other forms of interactions

Probenecid decreases the renal tubular secretions of Ampicillin and Sulbactam. Concurrent use of probenecid with SULBACIN may result in increased and prolonged blood levels of Ampicillin and Sulbactam.

The concurrent administration of Allopurinol and Ampicillin increases substantial the incidences of rashes in patients receiving both drugs as compared to patients receiving

Ampicillin alone. It is known whether this potentiation of Ampicillin rashes is due to allopurinol or the hyperuricemia present in these patients. There are no data with SULBACIN and the allopurinol administered concurrently. SULBACIN and aminoglycosides should not be reconstituted together due to the in-vitro inactivation of aminoglycosides by the Ampicillin component of SULBACIN.

4.6 Pregnancy and lactation

Pregnancy

Reproduction studies have been performed in mice, rats and rabbits at doses upto ten (10) times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to SULBACIN. 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 (See Drug/Laboratory Test Interactions).

Labour and Delivery

Studies in guinea pigs have shown that intravenous administration of Ampicillin decreased the uterine tone, height and duration of contraction. However, it is not known whether the use of SULBACIN in human during labour or delivery has immediate or delayed adverse effects on the fetus, prolongs the duration of labour, or increases the likelihood that forceps delivery or other obstetrical intervention or resuscitation of the newborn will be necessary.

Nursing Mothers

Low concentrations of Sulbactam and Ampicillin are excreted in the milk, therefore, caution should be exercised when SULBACIN is administered to a nursing mother.

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4.7 Effects on ability to drive and use machine

No studies on the ability to drive and use machines under influence of ampicillin and sulbactam have been carried out. However, due to side effects reactivity may be decreased. Do not drive if feel affected.

4.8 Undesirable effects

SULBACIN is generally well tolerated. The following adverse reactions have been reported.
LOCAL ADVERSE REACTIONS: Patients with low pain threshold may complain of pain at the site of injection.

Pain at IM Injection site	16 %
Pain at IV Injection site	3 %
Thrombophlebitis	3 %

SYSTEMIC ADVERSE REACTION: Adverse reactions were diarrhoea in 3 % of the patients and rash in less than 2 % of the patients. Additional systemic reactions reported in literature in less than 1 % of the patients were itching, nausea, vomiting, candidiasis, fatigue, malaise, headache, chest pain, flatulence, abdominal distension, glossitis, urine retention, dysuria, edema, facial swelling, erythema, chills, tightness in throat, substernal pain, epistaxis and mucosal bleeding.

The following adverse reactions have been reported with Ampicillin class antibiotics and can also occur with SULBACIN.

Gastrointestinal: Gastritis, Stomatitis, black hairy tongue, enterocolitis and psuedomembranous colitis. Occasionally, elevation in liver enzyme levels have been reported which revert to normal on discontinuation of the drug.

Hypersensitivity Reactions: Urticaria, erythea multiforme and occasional case of exfoliative

dermatitis have been reported. These reactions may be controlled with antihistamines and if necessary systemic corticosteroids. Whenever such reactions occur, the drug should be discontinued, unless the opinion of the physician dictates otherwise. Serious and occasional fatal hypersensitivity (anaphylactic) reactions can occur with penicillin.

Hematologic: In addition to adverse laboratory changes like fall in hemoglobin levels, hematocrit and increase in leucocyte count has been reported during therapy with penicillins. All of these reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena.

4.9 Overdose and special antidotes

Neurological adverse reactions, including convulsions, may occur with the attainment of high CSF levels of beta-lactams. Ampicillin may be removed from circulation by hemodialysis. The molecular weight ,degree of protein binding and pharmacokinetics profile of Sulbactam suggest that this compound may also be removed by hemodialysis.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

Microbiology: A wide range of beta-lactamases found in microorganisms resistant to penicillins and cephalosporins have been shown to be irreversibly inhibited by Sulbactam. Although Sulbactam alone possesses little useful antibacterial activity, it is effective against the Neisseriaciae. Whole organism studies have shown that Sulbactam restores Ampicillin's activity against beta-lactamase producing strains. In particular, Sulbactam has good inhibitory activity against the clinically important plasmid mediated beta-lactamases most frequently responsible for transferred drug resistance. Sulbactam has no deleterious effect on the activity of Ampicillin against Ampicillin susceptible strains.

The presence of Sulbactam in the SULBACIN formulation effectively extends the antimicrobial spectrum of Ampicillin to include many bacteria normally resistant to it and to

other beta-lactam antibiotics. Thus, Sulbacin possesses the synergistic properties of a broad spectrum antibiotic and beta-lactamase inhibitor.

The bactericidal activity of Ampicillin has been demonstrated against susceptible organisms during the stage of active multiplication. It inhibits cell wall mucopeptide biosynthesis.

Ampicillin has a broad-spectrum bactericidal activity against many gram positive and gram negative aerobic and anaerobic bacteria. Ampicillin is, however, degraded by beta-lactamases and therefore, the spectrum of activity does not normally include beta-lactamase producing organisms.

Microorganisms susceptible to Sulbacin: Gram-Positive Bacteria: Staphylococcus aureus (beta-lactamase producing) and Staphylococcus epidermidis (beta-lactamase and non- beta-lactamase producing), Staphylococcus saprophyticus (beta-lactamase and non- beta-lactamase producing), Streptococcus faecalis* (Enterococcus), Streptococcus pneumoniae* (formally D. pneumoniae), Streptococcus pyogens*, Streptococcus viridans*.

***Gram-Negative Bacteria*:** Hemophilus influenza (beta-lactamase and non - beta-lactamase producing), Branhamella catarrhalis (formally Neisseria catahalis) (beta-lactamase and non-beta-lactamase producing), Klebsialla species (all known strains are beta-lactamase producing), Proteus vulgaris, Providencia stuarti, Morganella morganii and Neisseria gonorrhoeae (beta-lactamase and non- beta-lactamase producing).

Anaerobes: Clostridium species*, Peptococcus species*, Bacteroides species including B. fragilis. (*- These are not beta-lactamase producing strains and therefore, are susceptible to ampicillin alone).

5.2 Pharmacokinetic Properties

General: Peak serum levels of Sulbactam / Ampicillin are achieved within 15 minutes after completion of infusion of SULBACIN I.V. or after 30-60 minutes following I.M. administration. Serum concentrations are dependent upon the dose of the drug used, the route

and body weight of the patient.
The mean serum half-life of both is approximately one hour in healthy volunteers.
Approximately 75 to 85% of both Sulbactam and Ampicillin are excreted unchanged in the urine during the first 8 hours after administration of SULBACIN to individuals with normal renal function.

In patients with impaired renal function the elimination kinetics of Sulbactam and Ampicillin are similarly affected, hence the ratio of one to the other remains constant whatever the renal function. The dose of SULBACIN (Sulbactam Sodium/Ampicillin Sodium) in such patients should be administered in accordance with the usual practice for Ampicillin.

Ampicillin is approximately 28% reversibly bound to human serum protein and Sulbactam is approximately 38% reversibly bound. SULBACIN penetrates readily into the various tissues and body fluids like peritoneal fluid, intestinal mucosa, appendix etc. and offers synergistic actericidal concentration.

Penetration of both Sulbactam and Ampicillin into cerebrospinal fluid in the presence of inflamed meninges has been demonstrated after IV administration of SULBACIN.

5.3 Preclinical Safety Data
Long-term studies in animals have been not been performed to evaluate carcinogenic or mutagenic potential.

6. Pharmaceutical Particulars

6.1 List of excipients : Not applicable

6.2 Incompatibilities :
SULBACIN sterile powder is to be stored at or below 30°C prior to reconstitution.

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When concomitant therapy with aminoglycosides is indicated, SULBACIN and aminoglycosides should be reconstituted and administered separately, due to the in vitro inactivation of aminoglycosides by any of the aminopenicillins.

6.3 Shelf life: 24 Months

6.4 Special precautions for storage :

Store below 30°C. Protected from light and moisture. Keep all medicines out of reach of children.

6.5 Nature and contents of container :

10 ml colourless glass vial with 20 mm standard neck. This vial is closed with grey butyl rubber plug and further sealed with burgundy aluminium flip off seal

7. Marketing Authorization Holder

Unichem Laboratories Limited,
Unichem Bhavan
Prabhat Estate, S.V. Road
Jogeshwari (West)
Mumbai - 400 102
INDIA.

8. Manufacturer's Name

Unichem Laboratories Limited
Unit I, Village Bhatauli Kalan,
Baddi (H.P) – 173 205, India.
+91-01795-246702/06, 244507, 245322

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9. Date of first authorization/renewal of the authorization: Not applicable

10. Date of revision of the text: Not applicable

1.3.2 Labelling (primary and secondary packaging)

Enclosed overleaf Label and Carton for Sulbacin 0.75 (Ampicillin and Sulbactam For Injection USP)