Negacef

Ceftazidime Injection

Negacef sterile powder for injection is supplied as a white to light yellow powder in vials containing mixture of ceftazidime and sodium carbonate, which is added to facilitate the absorption. pH of the drug is 5 to 8.

Composition

Each vial contains ceftazidime equivalent to 0.5g or 1g and sodium carbonate equivalent to 60mg or 121mg.

Properties

Ceftazidime the active ingredient of **Negacef,** is a third-generation cephalosporin having a high degree of stability in the presence of beta-lactamases and, therefore, excellent activity against a wide spectrum of Gram-negative and Gram-positive bacteria.

Ceftazidime is bactericidal; it acts by inhibiting bacterial septum and cell wall synthesis. A wide range of pathogenic strains and isolates associated with hospital-acquired infections are susceptible to ceftazidime *in vitro*, including:

Gram-negative: *Pseudomonas aeruginosa* and other *Pseudomonas* spp., *Klebsiella pneumoniae* and other *Klebsiella* spp., *Proteus mirabilis, Proteus vulgaris, Morganella morganii, Proteus rettgeri, Providencia* spp., *E. coli, Enterobacter* spp., *Citrobacter* spp., *Serratia* spp., *Salmonella* spp., *Shigella* spp., *Yersinia enterocolitica, Pasteurella multocida, Acinetobacter* spp., *Neisseria gonorrhoeae, Neisseria meningitidis, H. influenzae, H. parainfluenzae.*

Gram-positive: *Staphylococcus aureus* (methicillin-sensitive strains), *Staphylococcus epidermidis* (methicillin-sensitive strains), *Micrococcus* spp., *Streptococcus pyogenes, Streptococcus* group B, *Streptococcus pneumoniae, Streptococcus mitis,* and other *Streptococci.*

Anaerobic Strains: *Peptococcus* spp., *Peptostreptococcus* spp., *Streptococcus* spp., *Propionibacterium* spp., *Clostridium perfringens, Fusobacterium* spp., *Bacteroides* spp.

Ceftazidime is not active *in vitro* against methicillin–resistant *Staphylococci, Streptococcus faecalis,* and many other *Enterococci, Listeria monocytogenes, Campylobacter* spp., or *Clostridium difficile.*

In vitro the activities of ceftazidime and aminoglycosides in combination have been found to be at least additive; there is evidence of synergy in some strains tested. This property may be important in the treatment of febrile neutropenic patients.

Indications

Negacef is indicated for the treatment of single infections and for mixed infections caused by two or more susceptible organisms. Ceftazidime, because of its broad antibacterial spectrum, may be used alone as first choice drug, pending sensitivity test results. In meningitis, it is recommended that the results of a sensitivity test are known before treatment with ceftazidime as a single agent.

Negacef is effective in the treatment of:

1. Severe infections in general: e.g., septicaemia, bacteraemia, peritonitis, meningitis, infections in immunosuppressed patients with haematological or solid malignancies, and in patients in intensive care units with specific problems, e.g., infected burns.
2. Respiratory tract infections: e.g., pneumonia, broncho-pneumonia, infected pleurisy, empyema, lung abscess, infected bronchiectasis, and bronchitis, as well as in lung infections in patients with cystic fibrosis.
3. Ear, nose, and throat infections: e.g., otitis media, malignant otitis externa, mastoiditis, sinusitis, and other severe ear and throat infections.
4. Urinary tract infections: e.g., acute and chronic pyelonephritis, pyelitis, prostatitis, cystitis, urethritis (bacterial only), renal abscess, and infections associated with vesical and renal stones.
5. Skin and soft tissue infections: e.g., erysipelas, abscesses, cellulitis, infected burns and wounds, mastitis, and skin ulcers.
6. Gastrointestinal, biliary and abdominal infections: e.g., cholangitis, cholecystitis, empyema of gall bladder, intra-abdominal abscesses, peritonitis, diverticulitis, enterocolitis, post-partum, and pelvic inflammatory conditions.
7. Bone and joint infections: e.g., osteitis, osteomyelitis, septic arthritis, and infected bursitis.
8. Dialysis: infections associated with haemo- and peritoneal dialysis and with continuous ambulatory peritoneal dialysis (CAPD).

Dosage and Administration

Negacef is to be used by the parenteral route, the dosage depends upon the severity, sensitivity, and type of infection as well as the age, weight, and renal function of the patient.

Adults: The adult dosage range for **Negacef** is 1 to 6g per day; for instance, 500mg, 1g, or 2g given 12- or 8-hourly by IV or IM injection. In urinary tract infections and in many less serious infections, 500mg or 1g 12-hourly is usually adequate. In the majority of infections, 1g 8-hourly or 2g 12-hourly should be given. In very severe infections, especially in immunocompromised patients, including those with neutropenia, 2g 8- or 12-hourly should be administered.

Cystic fibrosis: In fibrocystic adults who have pseudomonal lung infections, high doses of 100 to 150mg/kg/day as three divided doses should be used. 9g/day has been used safely.

Infants and children: The usual dosage range for children aged over two months is 30 to 100mg/kg/day, given as two or three divided doses. Doses up to 150mg/kg/day (maximum 6g daily) in three divided doses may be given to infected immunocompromised or fibrocystic children or children with meningitis.

Neonates and children up to 2 months of age: Whilst clinical experience is limited, a dose of 25 to 60mg/kg/day given as two divided doses has proved to be effective. In the neonates, the serum half-life of ceftazidime can be three to four times that in adults.

Dosage in impaired renal function: Ceftazidime is excreted by the kidneys almost exclusively by glomerular filtration; therefore, dosage adjustment is required in patients with impaired renal function. A recommended regimen is as follows:

Creatinine clearance (mL/min)	Recommended unit dose of ceftazidime (g)	Frequency of dosing (hourly)
31-50	1.0	12
16-30	1.0	24
6-15	0.5	24
≤ 5	0.5	48

In patients with severe infections, especially in neutropenics, who would normally receive a dose of 6g ceftazidime daily, which is not for renal insufficiency, the unit dose given in the table above may be increased by 50% or the dosing frequency increased appropriately. In such patients it is recommended that ceftazidime serum levels should be monitored and trough levels should not exceed 40mg/L.

Dosage in peritoneal dialysis: **Negacef** may also be used in peritoneal dialysis and continuous ambulatory peritoneal dialysis (CAPD). As well as using **Negacef** intravenously, it can be incorporated into the dialysis fluid (usually 125 to 250mg for 2L of dialysis fluid).

Administration

Negacef is administered intramuscularly or intravenously. For intramuscular administration, **Negacef** should be reconstituted with either sterile water for injection, or 0.5% or 1.0% Lidocaine Hydrochloride injection. For direct intermittent intravenous administration, reconstitute with sterile water for injection.

Vial Size	Amount of Diluent to be added (mL)		
	Intramuscular	Intravenous	Intravenous infusion
0.5g	1.5	5	–
1g	3	10	50

Note: To preserve product sterility, it is important that a gas relief needle is not inserted through the vial closure before the product has dissolved.

These solutions may be given directly into the vein or introduced into the tubing of a giving set if the patient is receiving parenteral fluids. Ceftazidime is compatible with the most commonly used intravenous fluids.

Contraindications, Warnings, etc.

Contraindications: Ceftazidime is contraindicated in patients with known hypersensitivity to cephalosporin antibiotics.

Warnings: As with other beta-lactam antibiotics, before therapy with ceftazidime is instituted, careful inquiry should be made for a history of hypersensitivity reactions to ceftazidime, cephalosporins, penicillins, or other drugs.

Precautions: Cephalosporin antibiotics at high dosage should be given with caution to patients receiving concurrent treatment with nephrotoxic drugs, e.g., aminoglycoside antibiotics, or potent diuretics such as frusemide, as these combinations are suspected of adversely affecting renal function. Clinical experience with ceftazidime has shown that this is not likely to be a problem at the recommended dose levels.

There is no experimental evidence of embryopathic or teratogenic effects attributable to ceftazidime but, as with all drugs, it should be administered with caution during the early months of pregnancy and in early infancy. Use in pregnancy requires the anticipated benefit be weighed against the possible risks. Ceftazidime is excreted in human milk in low concentrations and consequently caution should be exercised when ceftazidime is administered to a nursing mother.

Ceftazidime does not interfere with enzyme-based tests for glycosuria. Slight interference with copper reduction methods (Benedict's, Fehling's, Clinitest) may be observed. Ceftazidime does not interfere in the alkaline picrate assay for creatinine. The development of a positive Coombs' test associated with the use of ceftazidime in about 5% of patients may interfere with the cross-matching of blood.

As with other broad-spectrum antibiotics, prolonged use of ceftazidime may result in the overgrowth of non-susceptible organisms (e.g., Candida, Enterococci) which may require interruption of treatment or adoption of appropriate measures.

Side Effects

Clinical trial experience has shown that ceftazidime is generally well-tolerated.

Adverse reactions are infrequent and include:

Local: phlebitis or thrombophlebitis with IV administration; pain and/or inflammation after IM injection.

Hypersensitivity: maculopapular or urticarial rash, fever, pruritus, and very rarely angioedema and anaphylaxis.

Gastrointestinal: diarrhoea, nausea, vomiting, abdominal pain, and very rarely oral thrush or colitis.

Other less frequent side effects include headache, dizziness, and paraesthesia. Convulsions have been reported in few cases with high doses.

Laboratory test changes noted transiently during ceftazidime therapy include: eosinophilia, positive Coombs' test without haemolysis, thrombocytosis and slight elevations in one or more of the hepatic enzymes ALT (SGOT), AST (SGPT), LDH, GGT, and alkaline phosphatase.

As with some other cephalosporins, transient elevations of blood urea, blood urea nitrogen, and/or serum creatinine have been observed occasionally.

Overdosage

Serum levels of ceftazidime are reduced by dialysis.

Pharmaceutical precautions

Vials of **Negacef** for injection as supplied are under reduced pressure; a positive pressure is produced on reconstitution due to the release of carbon dioxide.

Occasional storage at temperatures not higher than 30°C for up to 2 months is not detrimental to the product.

Vials of **Negacef** for injection do not contain any preservatives and should be used as single-dose preparations.

In keeping with good pharmaceutical practice, it is preferable to use freshly constituted solutions of **Negacef** for injection. If this is not practicable, satisfactory potency is retained for 18 hours at room temperature (below 25°C) or for 7 days if refrigerated when prepared in Water for Injection BP or any of the injections listed below:

At ceftazidime concentrations between 1mg/mL and 40mg/mL in:

0.9% Sodium Chloride Injection BP.
M/6 Sodium Lactate Injection BP.
Compound Sodium Lactate Injection BP (Hartmann's Solution).
5% Dextrose Injection BP.
0.225% Sodium Chloride and 5% Dextrose Injection BP.
0.45% Sodium Chloride and 5% Dextrose Injection BP.
0.9% Sodium Chloride and 5% Dextrose Injection BP.
0.18% Sodium Chloride and 4% Dextrose Injection BP.
10% Dextrose Injection BP.
Dextran 40 Injection BP 10% in 0.9% Sodium Chloride Injection BP.
Dextran 40 Injection BP 10% in 5% Dextrose Injection BP.
Dextran 70 Injection BP 6% in 0.9% Sodium Chloride Injection BP.
Dextran 70 Injection BP 6% in 5% Dextrose Injection BP.
(Ceftazidime is less stable in Sodium Bicarbonate Injection than in other intravenous fluids; therefore, Sodium Bicarbonate Injection is not recommended as a diluent.).

At concentrations between 0.05mg/mL and 0.25mg/mL in:

Intraperitoneal Dialysis Fluid (Lactate) BPC 1973.

When reconstituted for intramuscular use with:

0.5% OR 1% Lidocaine Hydrochloride Injection BP.

When admixed at 4mg/mL with:

(both components retain satisfactory potency)
Hydrocortisone (hydrocortisone sodium phosphate) 1mg/mL in 0.9% Sodium Chloride Injection BP or 5% Dextrose Injection BP.
Cefuroxime (Cefuroxime sodium) 3mg/mL in 0.9% Sodium Chloride Injection BP.
Cloxacillin (cloxacillin sodium) 4mg/mL in 0.9% Sodium Chloride Injection BP.
Heparin 10u/mL or 50u/mL in 0.9% Sodium Chloride Injection BP.
Potassium Chloride 10mEq/L in 0.9% Sodium Chloride Injection BP.

Ceftazidime and aminoglycosides should not be mixed in the same giving set or syringe.

Solutions range from light yellow to amber depending on concentration, diluent, and storage conditions used. Within the stated recommendations, product potency is not adversely affected by such colour variations.

Precipitation has been reported when vancomycin has been added to ceftazidime in solution. Therefore, it would be prudent to flush giving sets and intravenous lines between the administration of these two agents.

Presentation

Negacef sterile powder for injection is available in vials containing 0.5g and 1g ceftazidime.

* *Store at room temperature not exceeding 25°C, away from heat and light.*

THIS IS A MEDICAMENT

- Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of the reach of the children.

Council of Arab Health Ministers, Union of Arab Pharmacists.

Revised date : 01/09/1999