

Rx For the use of a Registered Medical Practitioner or a Hospital or a Laboratory Only

Aztreonam for Injection USP 1gm AZETRIM 1

Composition:

Each Vial Contains:

Aztreonam USP (Sterile)

equivalent to

Anhydrous Aztreonam500mg
(added L-arginine as buffer)

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DESCRIPTION:

Aztreonam contains which is a synthetic bactericidal antibiotic belonging to a new family of antibacterials - the monobactams - that was originally isolated from chromobacterium violaceum. The monobactams have a unique beta-lactam antibiotics (e.g. penicillins, cephalosporins). The sulphonic acid substitute in the 1-position of the ring activates the beta-lactam moiety, an aminothiazolyl oxime side chain in the 3-position and methyl group in the 4-position confer the specific antibacterial spectrum and beta-lactamase stability. Aztreonam is designated chemically as (Z)-2-[[[2-amino-4thiazolyl] [2 S, 3 S]-2-methyl-4-oxo-1-sulfo-3-azetidinyl] carbamoyl] methylene amino]oxy]-2-methyl-propionic acid. It has a structural formula of $C_{16}H_{18}N_4O_6S_2$ with a molecular weight of 435.44.

PHARMACOKINETICS:

Aztreonam is poorly absorbed from the gastrointestinal tract and is therefore administered parenterally. Absorption after intramuscular injection is good, peak plasma concentration of about 46 mg per ml have been achieved within one hour of a 1gm dose. Aztreonam has plasma half life of approximately 1.7 hours. The half life may be prolonged in neonates in renal impairment. About 56% of the drug in body in circulation is bound to plasma proteins. It is widely distributed in body tissues and fluid, including bile. Diffusion in to the CSF is poor unless the meninges are inflamed. It crosses the placenta and enters the fetal circulation; small amounts are distributed in breast milk. Aztreonam is not extensively metabolized. The principle metabolite, S-26992, is in active and is formed by opening of beta lactam ring; it has a much longer half life than the parent compound. Aztreonam is excreted predominantly in the urine, by renal tubular secretion in 8 hours as unchanged drug with only small quantity of metabolites, only small amounts of unchanged drug and metabolites are excreted in this faces.

ANTIMICROBIAL ACTION

Aztreonam is bactericidal and acts similarly to the penicillins by inhibiting synthesis of the bacterial cell wall; it has a high affinity for the penicillin-binding protein (PBP-3) of Gram-negative bacteria. The activity of Aztreonam is restricted to Gram-negative aerobic organism. It is active against most Enterobacteriaceae including Escherichia coli, Klebsiella, proteus, Providencia, Salmonella, Serratia, Shigella, and Yersinia spp. Most of these organisms are inhibited in vitro by a concentration of Exocute of 4 ug or less per ml. Some strains of Enterobacter and

Citrobacter spp are resistance. Aztreonam is active against Pseudomonas aeruginosa with MICs of 16 ug or less per ml. Most strains of other Pseudomonas spp. are insensitive. Aztreonam has good activity against Haemophilus Influenzae and Neisseria spp.; most strains are inhibited by concentrations of 0.5 ug or less per ml.

Aztreonam is stable to hydrolysis by many beta-lactamases and appears to be a poor inducer of beta-lactamase production. Acquired resistance has occasionally been reported.

INDICATIONS:

Aztreonam is indicated for the treatment of the following infections caused by susceptible gram-negative microorganisms.

- Urinary tract infections (complicated & uncomplicated)
- Lower respiratory tract infections
- Septicemia
- Skin and skin structure infections
- Intra-abdominal infections
- Gynaecological infections

CONTRAINDICATIONS:

Aztreonam is contraindicated in patients with known hypersensitivity of Aztreonam or any other component in the formulation.

PRECAUTIONS AND WARNINGS:

While cross-reactivity of Aztreonam with other beta-lactam antibiotics is rare, Aztreonam should be administered with caution to any patient with a history of hypersensitivity to betactams (e.g.: penicillins, cephalosporins, and or carbapenams). Treatments with Aztreonam can result in hypersensitivity reactions in patients with or without prior exposure to Aztreonam. If an allergic reaction to Aztreonam occurs, discontinue the drug and institute supportive treatment as appropriate (e.g.: maintenance of ventilation, pressors amines, and antihistamines, corticosteroids). Serious hypersensitivity reactions may require epinephrine and other emergency measures.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including Aztreonam and many ranges in severity from mild to life threatening. Therefore it is important to consider this diagnosis in patients who present with diarrhea subsequent to administration of antibacterial agent. Mild cases pseudomembranous colitis usually responds to drug discontinues alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protons, supplementation, and treatment with an antibacterial drug clinically effective against C difficile. Rare cases of toxic epidermal necrolysis have been reported in association with Aztreonam in patients undergoing bone marrow transplant with multiple risk factors including sepsis, radiation therapy and other concomitantly administered drug association with toxic epidermal necrolysis. In patient with impaired hepatic or renal function, appropriate monitoring is recommended during therapy. The use of antibiotics may promote the overgrowth of non-susceptible organism, including gram-positive organism (Staphylococcus aureus and streptococcus faecalis) and fungi. Should super infection occur during therapy, appropriate measures should be taken.

DRUG INTERACTION:

Caution is recommended in patients receiving aztreonam and oral

anticoagulant therapy because of the possibility of increased prothrombin time. Concomitant administration of probenecid or furosemide and Aztreonam causes clinically insignificant increases in the serum levels of Aztreonam. Single dose intravenous pharmacokinetic studies have not shown any significant interaction between aztreonam and concomitantly administered gentamycin, nafcillin sodium, cephadrine, clindamycin or metronidazole. No reports of disulfiram-like reaction with alcohol ingestion have been noted.

USAGE IN PREGNANCY, LACTATION & CHILDREN:

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always of human response, Aztreonam should be used during pregnancy only if clearly needed. Aztreonam in excreted of concentration determined in simultaneously obtained maternal serum. Consideration in simultaneously obtained maternal serum. Consideration should be given to temporary discontinuation of nursing and use of formula feedings. The safety and effectiveness of Aztreonam has not been established in children less than 9 months of age.

ADVERSE REACTION:

The adverse effects of Aztreonam are similar to those of other beta lactams. Hypersensitivity reactions, including skin rashes, urticaria, eosinophilia, and rarely anaphylaxis, may occur in patients receiving Aztreonam, although it has been reported to be only weakly immunogenic. Gastrointestinal effects include diarrhea, nausea, vomiting and an abnormal taste. Phlebitis or thrombophlebitis has been reported after the intravenous administration of Aztreonam, and pain or swelling after intramuscular injection. Administration of Aztreonam may result in the overgrowth of non-susceptible organism, including gram-positive cocci. Pseudomembranous colitis may develop. Other adverse effects that have been reported with Aztreonam included jaundice and hepatitis, increases in liver enzymes. And prolongation of prothrombin and partial thromboplastin time.

OVERDOSAGE:

If necessary, Aztreonam may be cleared from the serum by haemodialysis and/or peritoneal dialysis.

DOSAGE AND ADMINISTRATION:

Aztreonam is usually administered parenterally by deep intramuscular injection or by slow intravenous injection over 3 to 5 minutes, or by intravenous infusion over 20 to 60 minutes. It is given to adults in doses ranging from 1 to 8 gm daily, administered in divided doses every 6 to 10 hours, according to the severity of the infection. Single doses over 1 gm should be administered by the intravenous route. Children may be given Aztreonam in a dose of 20 mg per kg bodyweight every 6 or 8 hours. For severe infections, children of 2 years or older may be given 50 mg per kg every 6 or 8 hours up to a maximum total daily dose 8 gm. Dosage should be reduced in patients with moderate to severe renal impairment. Patients with renal impairment may be given a usual initial dose followed by a maintenance dose adjusted according to their creatinine clearance; those with a clearance of 10 to 30 ml per minute, half the initial dose; less than 10 ml per minute, one-quarter of the initial dose. A supplementary dose of one-eighth of the initial dose may be given to patients undergoing haemodialysis after each dialysis session. The duration of therapy

depends on the severity of infection. Generally, Aztreonam should be continued for at least 48 hours after the patients becomes asymptomatic or evidence of bacterial eradication has been obtained. Persistent infection may require treatment for several weeks.

PREPARATION OF PARENTERAL SOLUTION:

Upon the addition of diluents to the container, Contents should be shaken immediately and vigorously. Reconstituted solution are not for multiple dose use, should be entire volume in the container not be used for a single dose and the unused solution must be discarded. Depending upon the concentration of Aztreonam and diluents are used, reconstituted Aztreonam yields a colorless to light straw yellow solution which may develop a slight pink tint on standing (potency is not affected). Parental drug product should be inspected visually for particulate matter and discoloration whenever solution and container permit. For Bolus IV Injection: The contents of an Aztreonam (Aztreonam for Injection USP) 15 ml capacity vial should be reconstituted with 6 to 10 ml Sterile Water for Injections IP. For Bolus IV Infusion: If the contents of a 15 ml capacity vial are to be transferred to an appropriate infusion solution, each gram of Aztreonam should be initially reconstituted with at least 3 ml Sterile Water for Injections IP. Further dilution may be obtained with one of the following intravenous infusion solution to a final concentration not exceeding 2 % w/v. Sodium chloride Injection USP, 0.9% w/v Lactated Ringer's Injection IP, Dextrose Injection USP, 5% or 10 % -Dextrose and Sodium Chloride Injection USP, 5% 0.9%, 5%, 0.45% or 5%; 0.5% -Mannitol Injection USP 5% or 10% For IM Injection: The contents of an Aztreonam 15 ml capacity vial should be reconstituted with at least 3 ml of appropriate diluents per gram Aztreonam. The following diluents may be used: Sterile Water for Injections IP- Sodium Chloride Injection IP 0.9%w/v.

STABILITY OF IV AND IM SOLUTION:

Aztreonam solution for IV infusion at concentration not exceeding 2% w/v must be used within 48 hours following reconstituted if kept at controlled room temperatures (59°-86°F/15°-30°C) or within seven days if refrigerated (36°-46°F/2°-8°C). Frozen Aztreonam infusion solution may be stored for up to three months at 4°F/-20°C; frozen solution may be thawed at controlled room temperature or by overnight refrigerator. Solution that have been thawed and maintained at controlled room temperature or under refrigeration should be used within 24 or 72 hours after removal from the freezer, respectively. Solution should be not be refrozen. Aztreonam solution at concentrations exceeding 2% w/v, except those prepared with Sterile Water for Injections IP or Sodium chloride Injection IP 0.9% w/v, should be used promptly after preparation: the two expected solution must be used within 48 hours if stored at controlled room temperatures or within seven days if refrigerated.

Presentation:

Azetrim is available in 20ml vial along with 10ml WFI IP, along with Patient information leaflet.

Storage: Store at temperature not exceeding 30°C. Protect from light. Do not freeze.

Keep out of reach of children.

Manufactured by:

zyphar's
Pharmaceuticals

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