Front 100x240 Back

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

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Aztreonam for Injection USP 1000mg

AZTRAM-1000

For IV & IM Use

COMPOSITION

Each vial contains

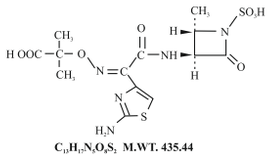
Aztreonam (Sterile) USP eq. to anhydrous Aztreonam	1000mg
(Added L-Arginine as buffer)	

DRUG DESCRIPTION

Aztreonam for injection USP contains the active ingredient, Aztreonam a monobactam. It was originally isolated from *Chromobacterium violaceum*. It is a synthetic bactericidal antibiotic. Monobactam antimicrobial drug for life-threatening infections with susceptible gram-negative aerobic organisms, especially *Pseudomonas aeruginosa*. Little activity against gram-positive or anaerobic bacteria. Aztreonam's unique molecular structure indicates that cross-reactivity between Aztreonam and other beta-lactams is very unlikely, thus it may be useful in the treatment of susceptible organisms in patients with penicillin or cephalosporin allergy.

The monobactams, having a unique monocyclic beta-lactam nucleus, are structurally different from other beta-lactam antibiotics (e.g., penicillins cephalosporins, cephamycins). The sulfonic acid substituent in the 1-position of the ring activates the beta-lactam moiety; an aminothiazolyl oxime side chain in the 3-position and a methyl group in the 4-Position confer the specific antibacterial spectrum and beta-lactamase stability.

Aztreonam is designated chemically as (Z)-2-[[[(2-amino-4-thiazolyl)[[(2S,3S)-2-methyl-4-oxo-1-sulfo-3-azetidinyl] carbamoyl]methylene]amino]oxy]-2-methylpropionic acid. Structural formula:



$C_{13}H_{17}N_5O_8S_2$ M.WT. 435.44

CLINICAL PHARMACOLOGY

Pharmacodynamics:

Like other β-lactam antibiotics, antibacterial activity results from inhibition of bacterial cell wall synthesis. Usually bactericidal, but not as rapidly bactericidal as some other β-lactam antibiotics (e.g., imipenem, cefotaxime, cefoxitin, ceftriaxone).

Pharmacokinetics:

Absorption: IM: Rapidly and completely absorbed following IM administration; peak serum concentrations generally attained within 1 hour after an IM dose. Peak serum concentrations attained with IM dose are slightly lower than those attained with equivalent IV dose, but serum aztreonam concentrations ≥ 1 hour after dosing are similar.

Distribution: IV or IM: Widely distributed into body tissues and fluids. Distributed into skeletal muscle, adipose tissue, skin, bone, gallbladder, liver, lungs, kidneys, atrial appendage, intestines, prostatic tissue, myometrium, endometrium, fallopian tubes, ovaries, and cervical and vaginal tissue. Also distributed into saliva, sputum,bronchial secretions, aqueous humor, and bile, and into pericardial, pleural,peritoneal, synovial, and blister fluids.

I***V:*** Distributed into CSF in adults and pediatric patients; CSF concentrations generally higher in patients with inflamed meninges than in those with uninflamed meninges. Crosses the placenta and is distributed into amniotic fluid.Distributed into milk in low concentrations.

Plasma Protein Binding: 46–60% bound to serum proteins in healthy adults at serum concentrations of 1–100 mcg/mL.

Adults with impaired renal function and decreased serum albumin concentrations: 22–49% bound to serum proteins.

Metabolism: Partially metabolized to several microbiologically inactive metabolites; no active metabolites have been found in serum or urine.

Elimination Route: Eliminated principally in urine as unchanged drug , Partially excreted in feces,presumably via biliary elimination.

Adults with normal renal and hepatic function: Distribution half-life averages 0.2–0.7 hours and elimination half-life averages 1.3–2.2 hours.

Children 2 months to 12 years of age: Elimination half-life averages 1.7 hours.

Neonates: Half-life is longer than in older children and adults and is inversely related to age and birthweight.15 In neonates <7 days of age, elimination half-life averages 5.5–9.9 hours in those weighing <2.5 kg5 15 and 2.6 hours in those weighing >2.5 kg.15 In neonates 1 week to 1 month of age, elimination half-life averages 2.4 hours.15

INDICATIONS & USAGE

Before initiating treatment with aztreonam, appropriate specimens should be obtained for isolation of the causative organism (s) and for determination of susceptibility to aztreonam. Treatment with aztreonam may be started empirically before results of the susceptibility testing are available; subsequently, appropriate antibiotic therapy should be continued.

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

Urinary Tract Infections (complicated and uncomplicated), including pyelonephritis and cystitis (initial and recurrent) caused by *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Enterobacter cloacae, Klebsiella oxytoca*, Citrobacter species* and Serratia marcescens**.

Lower Respiratory Tract Infections, including pneumonia and bronchitis caused by Escherichia coli, Klebsiella pneumoniae, *Pseudomonas aeruginosa, Haemophilus influenzae, Proteus mirabilis, Enterobacter species and Serratia marcescens**.

Septicemia caused by *Escherichia coli, Klebsiella pneumoniae*, Pseudomonas aeruginosa, Proteus mirabilis*, Serratia *marcescens* and Enterobacter species.*

Skin and Skin-Structure Infections, including those associated with postoperative wounds, ulcers and burns caused by *Escherichia coli, Proteus mirabilis, Serratia marcescens, Enterobacter species, Pseudomonas aeruginosa, Klebsiella pneumoniae and Citrobacter species**.

Intra-abdominal infections including peritonitis caused by Escherichia coli, Klebsiella species including K. pneumoniae, Enterobacter species including *E. cloacae*, Pseudomonas aeruginosa Citrobacter species* including C freundii* and Serratia species* including S. marcescens**.

Gynecologic Infections, including endometritis and pelvic cellulitis caused by Escherichia coli, Klebsiella pneumoniae*, Enterobacter species* including E. cloacae and proteus mirabilis*.

Surgery Aztreonam is indicated for adjunctive therapy to surgery in the management of infections caused by susceptible organisms, including abscesses, infections complicating hollow viscus perforations, cutaneous infections and infections of serous surfaces. Aztreonam is effective against most of the commonly encountered gram-negative aerobic pathogens seen in general surgery.

*Efficacy of this organism in this organ system was studied in fewer than ten infections.

Concurrent Therapy Concurrent initial therapy with other antimicrobial agents and aztreonam for injection, USP is recommended before the causative organism (s) is known in seriously ill patients who are also at risk of having an infection due to gram-positive aerobic pathogens. If anaerobic organisms are also suspected as etiologic agents, therapy should be initiated using an anti-anaerobic agent concurrently with aztreonam (see **DOSAGE AND ADMINISTRATION**). Certain antibiotics (e.g. cefoxitin, imipenem) may induce high levels of beta- lactamase in vitro in some gram-negative aerobes such as Enterobacter and pseudomonas species, resulting in antagonism to many beta-lactam antibiotics including aztreonam. These in vitro findings suggest that such betalactamase inducing antibiotics not be used concurrently with aztreonam.

DOSAGE & ADMINISTRATION

Dosage in Adult Patients

may be administered intravenously or by intramuscular injection. Dosage and route of administration should be determined by susceptibility of the causative organisms, severity and site of infection, and the condition of the patient.

The intravenous route is recommended for patients requiring single doses greater than 1g or those with bactrial septicemia, localized parenchymal abscess (e.g., intra-abdominal abscess), peritonitis or other severe systemic or life-threatening infections. The duration of therapy depends on the severity of infection. Generally, aztreonam should be continued for at least 48 hours after the patient becomes asymptomatic or evidence of bacterial eradication has been obtained. Persistent infections may require treatment for several weeks. Doses smaller than those indicated should not be used.

Renal Impairment in Adult Patients

Prolonged serum levels of aztreonam may occur in patients with transient or persistent renal insufficiency. Therefore, the dosage of aztreonam should be halved in patients with estimated creatinine clearances between 10 and 30 ml/min 1.73 m^2 after an initial loading dose of 1g or 2g.

When only the serum creatinine concentration is available, the following formula (based on sex, weight, and age of the patient) may be used to approximate the creatinine clearance (Clcr). The serum creatinine should represent a steady state of renal function.

$$\text{Males : Clcr} = \frac{\text{weight (kg)} \times (140 - \text{age})}{72 \times \text{serum creatinine}}$$

Females : 0.85 x above value.

In patients with severe renal failure (creatinine clearance less than 10 ml/min/1.73 m^2). Such as those supported by hemodialysis, the usual dose of 500 mg, 1g or 2g should be given initially. The maintenance dose should be one-fourth of the usual initial dose given at the usual fixed interval of 6,8 or 12 hours. For serious or life- threatening infections, in addition to the maintenance doses, one-eighth of the initial dose should be given after each hemodialysis session.

dosage guidelines

TYPE OF INFECTION	DOSE	FREQUENCY (hours)
ADULTS		
Urinary tract infections	500mg or 1g IV / IM	8 or 12
Moderately severe systemic infections	1g or 2g IV / IM	8 or 12
Severe systemic or life-threatening infections	2g IV / IM	6 or 8
Maximum recommended dose is :	8g/day	
PEDIATRIC PATIENTS		
Mild to moderate infections	30mg/kg IV	8
Moderate to severe infections	30mg/kg IV	6 or 8
Maximum recommended dose is :	120mg/kg/day IV	

CAPD

Administer 25% of the usual dose at the usual interval.

Dosage in The Elderly

Renal status is a major determinant of dosage in the elderly; these patients in particular may have diminished renal function. Serum creatinine may not be an accurate determinant of renal status. Therefore, as with all antibiotics eliminated by the kidneys, estimates of creatinine clearance should be obtained, and appropriate dosage modifications made if necessary.

Dosage in Pediatric Patients

(Aztreonam for injection USP) should be administered intravenously to pediatric patients with normal renal function. There are insufficient data regarding intramuscular administration to pediatric patients or dosing in pediatric patients with renal impairment.

Because of the serious nature of infections due to Pseudomonas aeruginosa, dosage of 2g every six or eight hours is recommended, at least upon initiation of therapy, in systemic infections caused by this organism in adults.

Preparation of Parenteral solutions

Preparation for administration

Upon the addition of the diluent to the container, contents should be shaken immediately and vigorously. Constituted solutions are not for multiple-dose use; should the entire volume in the container not be used for a single dose, the unused solution must be discarded.

Intramuscular Administration

Aztreonam for Injection should be constituted with at least 3 mL of diluent per gram of aztreonam. is given by deep injection into a large muscle mass (such as the upper outer quadrant of the gluteus maximus or lateral part of the thigh).

may be diluted with Water for Injection or sodium chloride injection, or the corresponding bacteriostatic preparations containing either benzyl alcohol or parabens as preservatives.

Intravenous Administration

For bolus injection: The selected dose should be constituted with 6 to 10 mL of Water for Injection and the resulting solution slowly injected directly into the vein over a period of 3 to 5 minutes.

For infusion: Each gram of aztreonam supplied in 15 mL vials should be initially constituted with at least 3 mL of Water for Injection. The resulting initial solution should be diluted with an appropriate infusion solution to a final concentration not exceeding 2% w/v (at least 50 mL solution per gram aztreonam).

The infusion should be administered over a 20-60 minute period. A number of intravenous solutions may be used as diluents for the administration of aztreonam by intravenous infusion. These include sodium chloride injection, dextrose and mixed injections of sodium chloride and dextrose, Ringers and Lactated Ringers Injection, Water for Injection, Electrolyte Replacement Injections and Mannitol Injection.

DILUENTS

Sodium Chloride Injection, USP, 0.9%; Ringer's Injection, USP; Lactated Ringer's Injection, USP; Dextrose Injection, USP, 5% or 10%; Dextrose and Sodium Chloride Injection, USP, 5%:0.9%, 5%:0.45% or 5%:0.2%; Sodium Lactate Injection, USP (M/6 Sodium Lactate); Ionosol® B and 5% Dextrose; Isolyte® E; Isolyte® E with 5% Dextrose; Isolyte® M with 5% Dextrose; Normosol®-R; Normosol®-R and 5% Dextrose; Normosol®-M and 5% Dextrose; Mannitol Injection, USP, 5% or 10%; Lactated Ringer's and 5%; Dextrose Injection; Plasma-Lyte M and 5% Dextrose; 10% Travert Injection; 10% Travert and Electrolyte No. 1 Injection; 10% Travert and Electrolyte No. 2 Injection; 10% Travert and Electrolyte No. 3 Injection.

Admixtures With Other Antibiotics

Intravenous infusion solutions of not exceeding 2% w/v prepared with Sodium Chloride Injection, USP 0.9% or Dextrose Injection, USP 5%, to which clindamycin phosphate, gentamicin sulfate, tobramycin sulfate, or cefazolin sodium have been added at concentrations usually used clinically, are stable for up to 48 hours at room temperature or 7 days under refrigeration. Ampicillin sodium admixtures with aztreonam in Sodium Chloride Injection, USP 0.9% are stable for 24 hours at room temperature and 48 hours under refrigeration; stability in Dextrose Injection, USP 5% is 2 hours at room temperature and 8 hours under refrigeration.

Aztreonam-cloxacillin sodium and aztreonam-vancomycin hydrochloride admixtures are stable in Dianeal 137 (Peritoneal Dialysis Solution) with 4.25% Dextrose for up to 24 hours at room temperature.

Aztreonam is incompatible with nafcillin sodium, cephradine, and metronidazole.

Other admixtures are not recommended since compatibility data are not available.

CONTRAINDICATIONS

This preparation is contraindicated in patients with known hypersensitivity to aztreonam or any other component in the formulation.

WARNINGS & PRECAUTIONS

General

In patients with impaired hepatic or renal function, appropriate monitoring is recommended during therapy. If an aminoglycoside is used concurrently with aztreonam especially if high dosages of the former are used or if therapy is prolonged, renal function should be monitored because of the potential nephrotoxicity or ototoxicity of aminoglycoside antibiotics. Should superinfection or pseudomembranous colitis occur appropriate measures should be taken.

Carcinogenicity Mutagenicity & Fertility studies

Carcinogenicity studies in animals have not been performed. Genetic toxicology studies performed in vivo and in vitro with aztreonam in serveral standard laboratory models revealed no evidence of mutagenic potential at the chromosomal or gene level. Two-generation reproduction studies in rats at daily doses up to 20 times the maximum recommended human dose, prior to and during gestation and lactation, revealed no evidence of impaired fertility.

Pregnancy

Pregnancy Category B: There are no adequate and well-controlled studies in pregnant women. Aztreonam should be used during pregnancy only if clearly needed.

Nursing Mothers: Aztreonam is excreted in breast milk in concentrations that are less than 1 percent of concentrations determined in simultaneously obtained maternal serum; consideration should be given to temporary discontinuation of nursing and use of formula feedings.

Pediatric Use : The safety and effectiveness of intravenous Aztreonam (Aztreonam for injection, USP) have been established in the age groups 9 month to 16 years. Use of Aztreonam in these age groups is supported by evidence from adequate and well-controlled studies of Aztreonam in adults with additional efficacy, safety, and pharmacokinetic data from non-comparative clinical studies in pediatric patients. Sufficient data are not available for pediatric patients under 9 months of age or for the following treatment indications/pathogens : septicemia and skin and skin-structure infections (where the skin infection is believed or known to be due to H. influenzae type b). In pediatric patients with cystic fibrosis, higher doses of aztreonam may be warranted.

SIDE EFFECTS

Local reactions such as phlebitis/thrombophlebitis following IV administration, and discomfort/swelling at the Injection site following IM administration occurred at rates of approximately 1.9 percent and 2.4 percent, respectively.

Systemic reactions considered to be related to therapy or of uncertain etiology) occurring at an incidence of 1 to 1.3 percent include diarrhea, nausea and /or vomiting, and rash.

Hypersensitivity: anaphylaxis, angioedema, bronchospasm.

Hematologic: pancytopenia, neutropenia, thrombocytopenia, anemia, eosinophilia, leukocytosis, thrombocytosis.

Gastrointestinal: abdominal cramps; rare cases of C. difficile-associated diarrhea, including pseudomembraneous colitis, or gastrointestinal bleeding have been reported.

Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment.

Dematologic: Toxic epidermal necrolysis, purpura, erythema multiforme, exfoliative dermatitis, urticaria, petechiae, pruritus, diaphoresis.

Cardiovascular: Hypotension, transient ECG changes (ventricular bigeminy and PVC), flushing.

Respiratory: Wheezing, dyspnea, chest pain.

Hepatobiliary: Hepatitis, jaundice.

Nervous System: Seizure, confusion, vertigo, paresthesia, insomnia, dizziness.

Musculoskeletal: Muscular aches.

Special Senses: Tinnitus, diplopia, mouth ulcer, altered taste, numb tongue, sneezing nasal congestion, halitosis.

Other: Vaginal candidiasis, vaginitis, breast tenderness.

Body as a Whole: Weakness, headache, fever, malaise.

Storage:
Store at or below 25°C.
Protect from light & moisture.

PRESENTATION

Available in individual cartons with package insert.

Mfg. by:-
Protech Telelinks
(A WHO- GMP Certified company)
Mauza-Ogli Suketi Road, Kala-Amb,
Distt. Sirmour- 173030 (H.P.)

Marketed by:

windlas

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