Atreon™

Aztreonam

COMPOSITION
Atreon™ 500: Each vial contains Aztreonam 500 mg as Aztreonam for injection USP (buffered with Arginine).
Atreon™ 1 gm: Each vial contains Aztreonam 1 gm as Aztreonam for injection USP (buffered with Arginine).
Atreon™ 2 gm: Each vial contains Aztreonam 2 gm as Aztreonam for injection USP (buffered with Arginine).

PHARMACOLOGY
The bactericidal action of Aztreonam results from the inhibition of bacterial cell wall synthesis due to a high affinity of Aztreonam for Penicillin Binding Protein 3 (PBP3). By binding to PBP3, Aztreonam inhibits the third and last stage of bacterial cell wall synthesis. Cell lysis is then mediated by bacterial cell wall autolytic enzymes such as autolysins.

Single 3-minute IV injections of 500 mg, 1 gm and 2 gm in healthy volunteers produced peak levels of 58, 125 and 242 mg/l. Peak levels of Aztreonam are achieved at about one hour after IM administration.

The serum half-life of Aztreonam averaged 1.7 hours in subjects with normal renal function, independent of the dose and route. In healthy subjects 60-70% of a single IM or IV dose was recovered in the urine by 8 hours, and urinary excretion was essentially complete by 12 hours.

INDICATION AND USAGE
Atreon is indicated in the treatment of the following infections caused by susceptible aerobic Gram-negative micro-organisms-
Urinary tract infections: Pyelonephritis, cystitis (initial and recurrent) and asymptomatic bacteriuria (including those due to pathogens resistant to the aminoglycosides, cephalosporins or penicillins).
Gonorrhea: Acute uncomplicated urogenital or anorectal infections.
Lower respiratory tract infections: Including pneumonia, bronchitis and lung infections in patients with cystic fibrosis.
Skin and soft tissue infections: Postoperative wounds, ulcers and burns.
Meningitis: Caused by *Haemophilus influenzae* or *Neisseria meningitidis*.
Gynecological infections: Pelvic Inflammatory Disease (PID), endometritis and pelvic cellulitis.
Intra-abdominal infections: Peritonitis.
Bacteremia/septicemia: Septicemia caused by *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis, Serratia marcescens* and Enterobacter species.
Bone and joint infections: Osteomyelitis, septic arthritis.

Aztreonam is also indicated for adjunctive therapy to surgery in the management of infections caused by susceptible organisms. Patients with serious Pseudomonas infections may benefit from concurrent use of Aztreonam and an aminoglycoside because of their synergistic action.

DOSAGE AND ADMINISTRATION
Adults
The usual dose of Aztreonam is 3 to 4 gm daily (maximum recommended dose is 8 gm daily). The dosage and route of administration should be determined by the susceptibility of the causative organisms, severity of infection and the condition of the patient.
In case of *Pseudomonas aeruginosa* infections, 2 gm every 6 or 8 hours is recommended.

Children
The usual dosage for patients older than one week is 30 mg/kg/dose every 6 or 8 hours. For severe infections in patients 2 years of age or older, 50 mg/kg/dose every 6 or 8 hours is recommended. Dosage information is not yet available for new-born less than 1 week old.

Dosage Guideline

Type of infections	Dose	Frequency (hours)
Adults*		
Urinary tract infections	500 mg or 1 gm	8 or 12
Moderately severe systemic infections	1 g or 2 gm	8 or 12
Severe systemic or life-threatening infections	2 gm	6 or 8
*Maximum recommended dose is 8 g per day.		
Pediatric patients**		
Mild to moderate infections	30 mg/kg	8
Moderate to severe infections (2 years or older)	50 mg/kg	6 or 8
**Maximum recommended dose is 120 mg/kg/day.		

Intramuscular administration
The dose should be given by deep injection into a large muscle mass. Aztreonam is well tolerated and should not be admixed with any local anesthetic agent.
For each gram of Aztreonam add at least 3ml water for injection BP and shake well.

Dose	Minimum volume of diluent to be added
0.5 gm	1.5 ml
1.0 gm	3.0 ml

Intravenous administration
A bolus injection may be used to initiate therapy. The dose should be slowly injected directly into a vein, or the tubing of a suitable administration set, over a period of 3 to 5 minutes.

Renal Impairment
In patients with impaired renal function, the normal recommended initial dose should be given. This should be followed by maintenance doses as shown in the following table:

Creatinine clearance (ml/min)	Maintenance dose
10 - 30	Half of the initial dose
Less than 10	One quarter of the initial dose

The normal dose interval should not be altered. In patients on haemodialysis, a supplementary one eighth of the initial dose should be given after each dialysis.
For infusion: Each gram of Aztreonam should be initially constituted with at least 3 ml of water for injection BP. The resulting 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 Aztreonam 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 etc.

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

PRECAUTION
Patients having hypersensitivity reactions to penicillins or cephalosporins should be treated with Aztreonam only if the potential benefit outweighs the potential risk of a severe allergic reaction. Antibiotic associated Pseudomembranous colitis has been reported with many antibiotics including Aztreonam.

Concurrent therapy with other antimicrobial agents and Aztreonam is recommended as initial therapy in seriously ill patients who are at risk of having an infection due to pathogens that are not susceptible to Aztreonam.

Appropriate monitoring of liver function in hepatic impaired patients is recommended during therapy.

ADVERSE REACTIONS
Aztreonam is generally well tolerated. In clinical studies following adverse effects were reported-
Hypersensitivity: Anaphylaxis, angioedema, bronchospasm.
Dermatologic: Rash; pruritus; petechiae; purpura; diaphoresis; flushing; urticaria; erythema multiforme; toxic epidermal necrolysis and exfoliative dermatitis.
Hematologic: Eosinophilia; increases in prothrombin and partial thromboplastin time; thrombocytosis, thrombocytopenia, leukocytosis, neutropenia, anemia, pancytopenia.
Hepatobiliary: Transient elevations of hepatic transaminases and alkaline phosphatase levels.
Gastrointestinal: Diarrhoea, nausea, vomiting; abdominal cramps, mouth ulcer and altered taste. Abdominal distension has been noted in children.
Rare cases of *C. difficile* -associated diarrhoea, including Pseudomembranous colitis, or gastro-intestinal bleeding have occurred.
Renal: Aztreonam was not associated with changes in renal function in healthy subjects.
Local Reactions: Discomfort at the IV injection site and phlebitis; mild discomfort was noted at IM injection site.
Miscellaneous: Following reactions were reported rarely: Vaginitis, candidiasis, hypotension, seizure, weakness, paraesthesia, confusion, dizziness, vertigo, insomnia, tinnitus, headache, breast tenderness, altered taste, muscle aches, fever, malaise, sneezing and nasal congestion.

DRUG INTERACTION
Concomitant administration of probenecid or furosemide and Aztreonam cause clinically insignificant increases in the serum levels of Aztreonam. Unlieke broad spectrum antibiotics, Aztreonam produced no effects on the normal anaerobic intestinal flora.

PREGNANCY AND LACTATION
Pregnancy
Pregnancy Category B. Aztreonam crosses the placenta and enters the fetal circulation. So it should be used during pregnancy only if the potential benefit justifies the potential risk.
Lactation
Aztreonam is excreted in breast milk in concentrations that are less than 1% of concentrations determined in simultaneously obtained maternal serum. Temporary discontinuation of nursing is recommended.

PEDIATRIC USE
Recommended for children of one week and older. Aztreonam for injection 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.

GERIATRIC USE
In the elderly, renal status is the major determinant of dosage. Estimated creatinine clearance should be used to determine appropriate dosage.

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

STORAGE
Store in a cool & dry place, protected from light & moisture. Keep all medicines out of reach of children.

HOW SUPPLIED
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Manufactured by :
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PHARMACEUTICALS LTD.
BANGLADESH
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