

neutropenia (3.2%), increased AST (3.8%), increased ALT (6.5%), and increased serum creatinine (5.8%).

In US pediatric clinical trials, neutropenia (absolute neutrophil count less than 1,000/mm³) occurred in 11.3% of patients (8/71) younger than 2 years receiving 30 mg/kg every 6 hours. AST and ALT elevations to greater than 3 times the upper limit of normal were noted in 15% to 20% of patients aged 2 years or above receiving 50 mg/kg every 6 hours. The increased frequency of these reported laboratory adverse events may be due to either increased severity of illness treated or higher doses of aztreonam for injection administered.

Adverse Laboratory Changes

Adverse laboratory changes without regard to drug relationship that were reported during clinical trials were:

Hepatic—elevations of AST (SGOT), ALT (SGPT), and alkaline phosphatase; signs or symptoms of hepatobiliary dysfunction occurred in less than 1% of recipients (see above).

Hematologic—increases in prothrombin and partial thromboplastin times, positive Coombs' test.

Renal—increases in serum creatinine.

OVERDOSAGE:

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

DOSAGE AND ADMINISTRATION:

Dosage in Adult Patients

Aztreonam for injection 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.

Table 4: Aztreonam for Injection Dosage Guidelines for Adults*

Type of Infection	Dose	Frequency (hours)
Urinary tract infections	500 mg or 1 g	8 or 12
Moderately severe systemic infections	1 g or 2 g	8 or 12
Severe systemic or life-threatening infections	2 g	6 or 8

* Maximum recommended dose is 8 g per day.

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

The intravenous route is recommended for patients requiring single doses greater than 1 g or those with bacterial 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 for injection 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 for injection should be halved in patients with estimated creatinine clearances between 10 and 30 mL/min/1.73 m² after an initial loading dose of 1 or 2 g.

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.

Males: Clcr =

weight
(kg)
×
(140
−
age)

72
×
serum
creatinine
(mg/dL)

{\displaystyle }

Females: 0.85 x above value

In patients with severe renal failure (creatinine clearance less than 10 mL/min/1.73 m²), such as those supported by hemodialysis, the usual dose of 500 mg, 1 g or 2 g 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 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 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 (see **PRECAUTIONS, Pediatric Use**).

Table 5: Aztreonam for Injection Dosage Guidelines for Pediatric Patients*

Type of Infection	Dose	Frequency (hours)
Mild to moderate infections	30 mg/kg	8
Moderate to severe infections	30 mg/kg	6 or 8

*Maximum recommended dose is 120 mg/kg/day.

CLINICAL STUDIES:

A total of 612 pediatric patients aged 1 month to 12 years were enrolled in uncontrolled clinical trials of aztreonam in the treatment of serious Gram-negative infections, including urinary tract, lower respiratory tract, skin and skin-structure, and intra-abdominal infections.

Preparation of Parenteral Solutions

General

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.

Depending upon the concentration of aztreonam and diluent used, constituted aztreonam for injection yields a colorless to light straw yellow solution which may develop a slight pink tint on standing (potency is not affected). Parenteral drug products should be inspected visually for particulate matter and discoloration whenever solution and container permit.

Admixtures with Other Antibiotics

Intravenous infusion solutions of aztreonam 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.

Intravenous Solutions

For Bolus Injection

The contents of an aztreonam for injection vial should be constituted with 6 to 10 mL Sterile Water for Injection, USP.

For Infusion

If the contents of a vial are to be transferred to an appropriate infusion solution, each gram of aztreonam should be initially constituted with at least 3 mL Sterile Water for Injection, USP. Further dilution may be obtained with one of the following intravenous infusion solutions:

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)

lonosol[®] 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

Intramuscular Solutions

The contents of an aztreonam for injection vial should be constituted with at least 3 mL of an appropriate diluent per gram aztreonam. The following diluents may be used:

Sterile Water for Injection, USP
Sterile Bacteriostatic Water for Injection, USP (with benzyl alcohol or with methyl- and propylparabens)
Sodium Chloride Injection, USP, 0.9%
Bacteriostatic Sodium Chloride Injection, USP (with benzyl alcohol)

Stability of Intravenous and Intramuscular Solutions

Aztreonam solutions for intravenous infusion at concentrations not exceeding 2% w/v must be used within 48 hours following constitution if kept at controlled room temperature (20° to 25°C/68° to 77°F, see USP) or within 7 days if refrigerated (2° to 8°C/ 36° to 46°F).

Aztreonam for Injection, USP, solutions at concentrations exceeding 2% w/v, except those prepared with Sterile Water for Injection, USP or Sodium Chloride Injection, USP, should be used promptly after preparation; the 2 excepted solutions must be used within 48 hours if stored at controlled room temperature or within 7 days if refrigerated.

Intravenous Administration

Bolus Injection

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 (see next paragraph regarding flushing of tubing).

Infusion

With any intermittent infusion of aztreonam and another drug with which it is not pharmaceutically compatible, the common delivery tube should be flushed before and after delivery of aztreonam with any appropriate infusion solution compatible with both drug solutions; the drugs should not be delivered simultaneously. Any aztreonam for injection infusion should be completed within a 20 to 60 minute period. With use of a *Y-type administration set*, careful attention should be given to the calculated volume of aztreonam solution required so that the entire dose will be infused. A volume control administration set may be used to deliver an initial dilution of aztreonam for injection (see **Preparation of Parenteral Solutions, Intravenous Solutions**, For Infusion) into a compatible infusion solution during administration; in this case, the final dilution of aztreonam should provide a concentration not exceeding 2% w/v.

Intramuscular Administration

The dose should be 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). Aztreonam is well tolerated and should not be admixed with any local anesthetic agent.

HOW SUPPLIED:

Aztreonam for Injection, USP

Product Code	Unit of Sale	Strength	Each
400120	63323-401-20 <p>Unit of 10</p>	1 g per vial	63323-401-01 <p>20 mL single dose vial</p>
400220	63323-402-20 <p>Unit of 10</p>	2 g per vial	63323-402-01 <p>30 mL single dose vial</p>

Storage

Store in original packages at 20° to 25°C (68° to 77°F)[see USP Controlled Room Temperature]; avoid excessive heat.

This container closure is not made with natural rubber latex.

REFERENCES:

- Naber KG, Dette GA, Kees F, Knothe H, Grobecker H. Pharmacokinetics, *in vitro* activity, therapeutic efficacy, and clinical safety of aztreonam vs. cefotaxime in the treatment of complicated urinary tract

infections. *J Antimicrob Chemother* 1986; 17:517-527.

2. Creasey WA, Platt TB, Frantz M, Suger-man AA. Pharmacokinetics of aztreonam in elderly male volunteers. *Br J Clin Pharmacol* 1985; 19:233-237.

3. Meyers BR, Wilkinson P, Mendelson MH, et al. Pharmacokinetics of aztreonam in healthy elderly and young adult volunteers. *J Clin Pharmacol* 1993; 33:470-474.

4. Sattler FR, Schramm M, Swabb EA. Safety of aztreonam and SQ 26,992 in elderly patients with renal insufficiency. *Rev Infect Dis* 1985; 7 (suppl 4):S622-S627.

5. Clinical and Laboratory Standards Institute (CLSI). Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard -Ninth Edition. CLSI document M07-A9, Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 2012.

6. National Committee for Clinical Laboratory Standards. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically*—Fifth Edition. Approved Standard NCCLS Document M7-A5, Vol. 20, No. 2, NCCLS, Wayne, PA, January 2000.

7. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Disk Diffusion Susceptibility Tests; Approved Standard – Eleventh Edition CLSI document M02-A11, Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 2012.

8. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing; Twenty-third Informational Supplement. CLSI document M100-S23, Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 2013.

9. Deger F, Douchamps J, Freschi E, et al. Aztreonam in the treatment of serious gram-negative infections in the elderly. *Int J Clin Pharmacol Ther and Toxicol* 1988; 26: 22-26.

10. Knockaert DC, Dejaeger E, Nestor L, et al. Aztreonam-flucloxacillin double beta-lactam treatment as empirical therapy of serious infections in very elderly patients. *Age and Aging* 1981; 20:135-139.

11. Roelands F. Clinical use of aztreonam in a psychogeriatric population. *Acta Clin Belg* 1992; 47:251-255.

12. Andrews R, Fasoli R, Scoggins WG, et al. Combined aztreonam and gentamicin therapy for pseudomonal lower respiratory tract infections. *Clin Therap* 1994; 16:236-252.

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