AZTREONAM FOR INJECTION, USP

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. The monobactams, having a unique monocyclic beta-lactam nucleus, are structurally different from other beta-lactam antibiotics (e.g., penicillins, cephalosporins, carbapenems). The sulfonic acid substituent in the 1-position of the ring activates the beta-lactam moiety; an aminothiazoyl 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-(2-amino-4-thiazoyl)][1-(25,35)-2-methyl-4-oxo-1-sulfo-3 azetidiny] carbamoyl]methylene] amino]oxy]-2-methylpropionic acid. Structural formula:

```
\[
\text{CH}_3 \quad \text{C} \quad \text{O} \quad \text{N} \quad \text{C} \quad \text{NH} \quad \text{H} \quad \text{H} \\
\text{H}_2\text{N} \quad \text{O} \quad \text{S} \quad \text{O} \text{H} \\
\text{C}_3\text{H}_7\text{N}_2\text{O}_5\text{S}_2 \\
\text{MW 435.44}
\]
```

Aztreonam for injection is a sterile, non-pyrogenic, sodium-free lyophilized, off-white to slightly yellow solid containing approximately 780 mg arginine per gram of aztreonam. Following constitution, the product is for intramuscular or intravenous use. Aqueous solutions of the product have a pH in the range of 4.5 to 7.5.

Each 500 mg contains 500 mg aztreonam with approximately 390 mg arginine.
Each 1 gram vial contains 1 gram aztreonam with approximately 780 mg arginine.
Each 2 gram vial contains 2 grams aztreonam with approximately 156 grams arginine.

CLINICAL PHARMACOLOGY:

- Single 30-minute intravenous infusions of 500 mg, 1 g and 2 g doses of aztreonam for injection in healthy subjects produced peak serum concentrations of 54, 80 and 204 mcg/mL, respectively, immediately after administration; at 8 hours, serum levels were 1, 3 and 6 mcg/mL, respectively (Figure 1).
- Single 3 minute intravenous injections of the same doses resulted in serum levels of 58, 125 and 242 mcg/mL at 5 minutes following completion of injection.
- Serum concentrations of aztreonam in healthy subjects following completion of single intramuscular injections of 500 mg and 1 g doses are depicted in Figure 1; maximum serum concentrations occur at about 1 hour. After identical single intravenous or intramuscular doses of aztreonam for injection, the serum concentrations of aztreonam are comparable at 1 hour (1.5 hours from start of intravenous injection) with similar slopes of serum concentrations thereafter.

**Figure 1**

<table>
<thead>
<tr>
<th>Aztreonam Serum Concentration (mcg/mL)</th>
<th>Hours</th>
<th>Number of Patients</th>
<th>Mean Serum Concentration (mcg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid or Tissue</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bilirubin fluid</td>
<td>1</td>
<td>IV</td>
<td>0.3</td>
</tr>
<tr>
<td>blister fluid</td>
<td>1</td>
<td>IV</td>
<td>0.4</td>
</tr>
<tr>
<td>bronchial secretion</td>
<td>2</td>
<td>IV</td>
<td>1.0</td>
</tr>
<tr>
<td>cerebrospinal fluid</td>
<td>2</td>
<td>IV</td>
<td>0.2</td>
</tr>
<tr>
<td>fluid (intravenous)</td>
<td>2</td>
<td>IV</td>
<td>0.1</td>
</tr>
<tr>
<td>renal failure</td>
<td>2</td>
<td>IV</td>
<td>0.3</td>
</tr>
<tr>
<td>synovial fluid</td>
<td>2</td>
<td>IV</td>
<td>0.8</td>
</tr>
<tr>
<td>Number of Patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Serum Concentration (mcg/mL)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

To reduce the development of drug-resistant bacteria and maintain the effectiveness of aztreonam for injection and other antibacterial drugs, aztreonam for injection should only be used to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

**EXTRAVASCULAR CONCENTRATIONS OF AZTREONAM AFTER A SINGLE PARENTERAL DOSE**

The level of aztreonam in serum was 1100 mcg/mL within the first 2 hours following a single 500 mg, 1 g and 2 g intravenous doses of aztreonam for injection (30 minute infusions), respectively. The range of average concentrations for aztreonam in the 8 to 12 hour urine specimens in these studies was 25 to 120 mcg/mL. After intramuscular injection of single 500 mg and 1 g doses of aztreonam for injection urinary levels were approximately 500 and 1500 mcg/mL, respectively, within the first 2 hours, declining to 180 and 470 mcg/mL in the 6 to 8 hour specimens. In healthy subjects, aztreonam is excreted in the urine in amounts that exceed the MIC90 for the same pathogens for up to 12 hours. When aztreonam pharmacokinetics were assessed for adult and pediatric patients, they were found to be comparable (down to 9 months old). The serum half-life of aztreonam averaged 1.7 hours (1.5 to 2) in subjects with normal renal function, independent of the dose and route of administration. In healthy subjects, based on a 70 kg person, the serum clearance was 91 mL/min and renal clearance was 56 mL/min; the apparent mean volume of distribution at steady-state averaged 12.6 liters, approximately equivalent to extracellular fluid volume.

In elderly patients, the mean serum half-life of aztreonam increased and the renal clearance decreased, consistent with the age-related decrease in creatinine clearance.

The dosage of aztreonam for injection should be adjusted accordingly (see DOSAGE AND ADMINISTRATION: Renal Impairment in Adult Patients).

In patients with impaired renal function, the serum half-life of aztreonam is prolonged (see DOSAGE AND ADMINISTRATION: Renal Impairment in Adult Patients). The serum half-life of aztreonam is only slightly prolonged in patients with hepatic impairment since the liver is a minor pathway of excretion.
The following in vitro data are available, but their clinical significance is unknown. Aztreonam exhibits in vitro minimal inhibitory concentrations (MICs) of 0.12 to 8 mcg/mL or less against most (≥90%) strains of the following microorganisms; however, the safety and effectiveness of aztreonam in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled clinical trials. **Aerobic gram-negative microorganisms:**

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>MIC (mcg/mL)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aeromonas hydrophila</td>
<td>ATCC 7966</td>
<td>0.25</td>
</tr>
<tr>
<td>Morganella morganii</td>
<td>ATCC 25986</td>
<td>0.12</td>
</tr>
<tr>
<td>Neisseria gonorrhoeae (including penicillinase-producing strains)</td>
<td>ATCC 6300</td>
<td>0.12</td>
</tr>
<tr>
<td>Pasteurella multocida</td>
<td>ATCC 25755</td>
<td>0.12</td>
</tr>
<tr>
<td>Proteus vulgaris</td>
<td>ATCC 27853</td>
<td>0.12</td>
</tr>
<tr>
<td>Providencia stuartii</td>
<td>ATCC 29426</td>
<td>0.12</td>
</tr>
<tr>
<td>Yersinia enterocolitica</td>
<td>ATCC 29472</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Aztreonam for Injection is indicated for the treatment of the following infections caused by certain gram-negative microorganisms: **Lower Respiratory Tract Infections**, including pneumonia and bronchitis caused by Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Enterobacter cloaceae, Klebsiella oxytoca, Citrobacter diversum, and Serratia marcescens.

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

**Intra-abdominal infections**, including perforated peptic ulcers, appendix, peritonitis, perforated peptic ulcer, and postoperative wound infections due to *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Serratia marcescens*.

**Septicemia** caused by *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus mirabilis*.

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

**Intra-abdominal infections**, including perforated peptic ulcers, appendix, peritonitis, perforated peptic ulcer, and postoperative wound infections due to *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Serratia marcescens*.

**Septicemia** caused by *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus mirabilis*.

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

**Septicemia** caused by *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus mirabilis*. **Intra-abdominal infections**, including perforated peptic ulcers, appendix, peritonitis, perforated peptic ulcer, and postoperative wound infections due to *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Serratia marcescens*.

**Septicemia** caused by *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus mirabilis*.
domonas aeruginosa, Citrobacter species* including C. freundii* and Serratia species* including S. marcescens.*

**Enterobacter** species* including Enterobacter cloacae, Klebsiella pneumoniae* and Proteus mirabilis.*

*Aztreonam for injection is indicated for adjunctive therapy to surgery in the management of infections caused by susceptible gram-negative aerobic pathogens seen in organisms, including abscesses, infections of the urinary tract, and skin and skin-structure infections (where the skin infection is believed or known to be due to *H. influenzae* or *S. pyogenes*). Suitable data are not available for pediatric patients under 9 months of age or for the following treatment indications: meningitis in adults with additional efficacy, safety, and pharmacokinetic data from non-comparative clinical studies in pediatric patients.

CONTRAINDICATIONS: Aztreonam for injection contains no sodium.

**ADVERSE REACTIONS:**

- **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% and 2.4%, respectively.
- **Systemic reactions (considered to be drug-related)** included diarrhea, nausea and/or vomiting, and rash.
- **Gastrointestinal**—diarrhea, nausea and/or vomiting, rash.
- **Hypersensitivity**—anaphylaxis, angioedema, bronchosospasm.
- **Hematologic**—pancytopenia, neutropenia, thrombocytopenia, anemia, eosinophilia, leukocytosis.
- **Gastrointestinal**—abdominal cramps; rare cases of *C. difficile*-associated diarrhea, including pseudomembranous colitis, or gastrointestinal bleeding have been reported. Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (see WARNINGS).
- **Dermatologic**—toxic epidermal necrolysis (see WARNING). Skin rashes, including Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, exfoliative dermatitis, urticaria, petechiae, pruritus, diaphoresis.
- **Special Senses**—tinnitus, diplopia, mouth ulcers, altered taste, numb tongue, sneezing.
- **Respiratory**—wheezing, dyspnea, chest pain.
- **Hepatobiliary**—hepatitis, jaundice.
- **Nervous System**—seizure, confusion, vertigo, paresthesia, insomnia, dizziness.
- **Musculoskeletal**—muscular aches.

**CLINICAL PHARMACOLOGY, DOSAGE AND ADMINISTRATION, AND CLINICAL STUDIES:**

Clinical studies of aztreonam for injection did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

In general, dose selection for an elderly patient should be guided by the same considerations applied to other patients requiring antibiotic therapy. In general, elderly patients should be treated with the same dose interval as younger patients, but the total daily dose should generally be reduced.

**Geriatric Use**

Aztreonam for injection contains no sodium.

**WARNINGS:**

Both animal and human data suggest that aztreonam is rarely cross-resistant with other beta-lactam antibiotics and weakly immunogenic. Treatment with aztreonam results 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, serum amines, antihistaminic corticosteroids). Serious hypersensitivity reactions may require epinephrine and other emergency measures (see ADVERSE REACTIONS).

- Occurrence of a difficulty associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including aztreonam for injection, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the gastrointestinal tract, and may promote overgrowth of nonsusceptible organisms, including *Clostridium difficile*, which can cause *C. difficile*-associated diarrhea, including pseudomembranous colitis, or gastrointestinal bleeding.

**Clinical Studies**

Aztreonam for injection has been reported to occur over two months after the administration of antibiotic agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be continued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and, if indicated, surgical evaluation should be instituted as clinically indicated.

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 drugs associated with toxic epidermal necrolysis.

**PRECAUTIONS:**

**Geriatric Use**

Aztreonam for injection contains no sodium.

**ADVERSE REACTIONS:**

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% and 2.4%, respectively.

Systemic reactions (considered to be drug-related) included diarrhea, nausea and/or vomiting, and rash. Reactions occurring at an incidence of less than 1% are listed within each body system in order of decreasing severity.

- **Hypersensitivity**—anaphylaxis, angioedema, bronchosospasm.
- **Gastrointestinal**—diarrhea, nausea and/or vomiting, rash.
- **Gastrointestinal**—abdominal cramps; rare cases of *C. difficile*-associated diarrhea, including pseudomembranous colitis, or gastrointestinal bleeding have been reported. Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (see WARNINGS).
- **Dermatologic**—toxic epidermal necrolysis (see WARNING). Skin rashes, including Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, exfoliative dermatitis, urticaria, petechiae, pruritus, diaphoresis.
- **Respiratory**—wheezing, dyspnea, chest pain.
- **Hepatobiliary**—hepatitis, jaundice.
- **Nervous System**—seizure, confusion, vertigo, paresthesia, insomnia, dizziness.
- **Musculoskeletal**—muscular aches.
less than 1% required discontinuation of therapy due to adverse events. The following are systemic adverse events, regardless of drug relationship, occurred in at least 1% of treated patients in domestic clinical trials: rash (4%), fever (1%). These adverse events were comparable to those observed in adult clinical trials.

In aztreonam patients receiving intravenous therapy, the following local reactions were noted: pain (12%), erythema (2.9%), induration (1.2%), and phlebitis (2.1%). In the US patient population, pain occurred in 1.5% of patients, while each of the remaining 3 local reactions occurred in an incidence of 0.5%.

The following laboratory adverse events, regardless of drug relationship, occurred in at least 1% of treated patients: increased eosinophils (6.3%), increased platelets (3.6%), neutropenia (3.3%), increased AST (5.9%), increased ALT (6.5%), and increased serum creatinine (5.8%).

In US pediatric clinical trials, neutropenia (absolute neutrophil count less than 1000/mm³) occurred in 11.3% of patients (6/71) younger than 1 year. Two patients were treated with an initial dose of 30 mg/kg, and one patient was treated with an initial dose of 50 mg/kg q8h. 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 infection administered.

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

Hepatic—elevation of ALT, alkaline phosphatase; signs of hyperbilirubinemia; deterioration of hepatic dysfunction in less than 1% of recipients (see above).

Neuropsychiatric—increases in prothrombin and partial thromboplastin times, positive Coombs’ test.

Constitution for IV infusion

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 the susceptibility of the causative organisms, severity and site of infection, and the condition of the patient.

IV route is recommended for patients requiring single doses greater than 1 g or those with bacterial septicaemia, localized abscess (e.g., intra-abdominal abscess), peritonitis or other severe systemic infections requiring admission.

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 renal insufficiency. Therefore, the dosage of aztreonam for injection should be halved in patients with creatinine clearance between 10 mL/min/1.73 m² and 30 mL/min/1.73 m² after an initial loading dose of 300 mg.

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 (Ccr). The serum creatinine should represent a steady state of renal function.

Male: Ccr = \( \frac{\text{weight (kg)}}{72 - \text{serum creatinine (mg/dL)}} \times 140 - \text{age} \)

Female: 0.85 \( \times \) 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 300 mg q12h should be given. One 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 the appropriate administration to pediatric patients or dosing in pediatric patients with renal impairment (see PRECAUTIONS: Pediatric Use).

Renal Impairment in Adult Patients

Prolonged serum levels of aztreonam may occur in patients with renal failure. Therefore, the dosage of aztreonam for injection should be halved in patients with creatinine clearance less than 10 mL/min/1.73 m², and 30 mL/min/1.73 m² after an initial loading dose of 300 mg.

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 (Ccr). The serum creatinine should represent a steady state of renal function.

Male: Ccr = \( \frac{\text{weight (kg)}}{72 - \text{serum creatinine (mg/dL)}} \times 140 - \text{age} \)

Female: 0.85 \( \times \) 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 300 mg q12h should be given. One 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 the appropriate administration to pediatric patients or dosing in pediatric patients with renal impairment (see PRECAUTIONS: Pediatric Use).

General

Upon the addition of the diluent to the container, contents should be inspected visually for particulate matter and discoloration whenever solution and container are used. The unused solution must be discarded.

Constitution for IV Infusion

The contents of aztreonam for injection vial should be constituted with at least 10 mL Sterile Water for Injection, USP, for infusion. Further dilution may be obtained with one of the following intravenous infusions:

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 0.5%, 0.2% Sodium Lactate Injection, USP (M/8 Sodium Lactate) Isotonic® B and 5% Dextrose Isolyte® E Isolyte® E with 5% Dextrose Isolyte® M with 5% Dextrose Normosol® R and 5% Dextrose Normosol® M and 5% Dextrose Mannitol Injection, USP, 5% or 10% Lactated Ringer’s and 5% Dextrose Injection PlasmaLyte® M and 5% Dextrose 10% Tr advant Injection 10% Tr advant and Electrolyte No. 1 Injection 10% Tr advant and Electrolyte No. 2 Injection 5% Dextrose Injection No. 3 Injection Intramuscular (IM) Solutions

Aztreonam for Injection for IM solution administration should be constituted as follows:

Intravenous (IV) Solutions

For Bolus Injection

Aztreonam for injection for IV bolus administration should be constituted as follows:

**CONSTITUTION FOR IV BOLUS**

<table>
<thead>
<tr>
<th>Strength</th>
<th>Vial size</th>
<th>Amount of Diluent to be added (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 mg/vial</td>
<td>20 mL</td>
<td>6 to 10</td>
</tr>
<tr>
<td>1 g/vial</td>
<td>20 mL</td>
<td>6 to 10</td>
</tr>
<tr>
<td>2 g/vial</td>
<td>30 mL</td>
<td>10</td>
</tr>
</tbody>
</table>

For Infusion

Aztreonam for injection for IV infusion should be constituted as follows:

**CONSTITUTION FOR IV INFUSION**

<table>
<thead>
<tr>
<th>Strength</th>
<th>Vial size</th>
<th>Initial Amount of Diluent to be added (mL)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 mg/vial</td>
<td>20 mL</td>
<td>1.5</td>
</tr>
<tr>
<td>1 g/vial</td>
<td>20 mL</td>
<td>3</td>
</tr>
<tr>
<td>2 g/vial</td>
<td>30 mL</td>
<td>6</td>
</tr>
</tbody>
</table>

*Further dilution required; see list of infusion solutions below.

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

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 0.5%, 0.2% Sodium Lactate Injection, USP (M/8 Sodium Lactate) Isotonic® B and 5% Dextrose Isolyte® E Isolyte® E with 5% Dextrose Isolyte® M with 5% Dextrose Normosol® R and 5% Dextrose Normosol® M and 5% Dextrose Mannitol Injection, USP, 5% or 10% Lactated Ringer’s and 5% Dextrose Injection PlasmaLyte® M and 5% Dextrose 10% Tr vant Injection 10% Tr vant and Electrolyte No. 1 Injection 10% Tr vant and Electrolyte No. 2 Injection 5% Dextrose Injection No. 3 Injection
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 (IV) 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

<table>
<thead>
<tr>
<th>Product</th>
<th>NDC No.</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>309720</td>
<td>63323-397-20</td>
<td>500 mg/vial 20 mL single dose vial, supplied in packages of ten.</td>
</tr>
<tr>
<td>400120</td>
<td>63323-401-20</td>
<td>1 g/vial 20 mL single dose vial, supplied in packages of ten.</td>
</tr>
<tr>
<td>400220</td>
<td>63323-402-20</td>
<td>2 g/vial 30 mL single dose vial, supplied in packages of ten.</td>
</tr>
</tbody>
</table>

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

REFERENCES:

Galaxy, Dianead, Plasma-Lyte, and Travert are registered trademarks of Baxter International, Inc. Isonol® and Normosol® are registered trademarks of Abbott Laboratories Corporation Isolyte® is a registered trademark of McGraw Inc.