

Monobactams

A monocyclic beta-lactam class represented in practice by aztreonam, active against aerobic gram-negative bacilli.

Online guide: <https://www.medguideglobal.com/pharmacology/antibiotics/monobactams>

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Quick revision

One Liner: Aztreonam is the monobactam: a monocyclic beta-lactam, parenteral, active mostly against aerobic gram-negative bacilli, and - uniquely among beta-lactams - not hydrolysed by metallo-beta-lactamases.

1. A synthetic monobactam with a monocyclic beta-lactam structure, originally isolated from *Chromobacterium violaceum*. [1]
2. Mechanism is the standard beta-lactam one: binds penicillin-binding proteins, inhibits cell-wall synthesis, decreases bacterial growth. [1]
3. Active mostly against gram-negative organisms, specifically aerobic gram-negative bacilli, and resistant to many beta-lactamases. [1]
4. In spectrum it more closely resembles the aminoglycosides than the penicillins. [1]
5. Class B metallo-beta-lactamases hydrolyse all beta-lactams except aztreonam - the single most examinable fact about this drug. [4]
6. Class A carbapenemases such as KPC do hydrolyse aztreonam, so the metallo-beta-lactamase exception is not a general one. [4]
7. Given parenterally; an inhalational formulation also exists. [1]

Overview

1. Aztreonam is a parenterally administered synthetic monobactam antibiotic. Where the penicillins and cephalosporins carry a beta-lactam ring fused to a second ring, the monobactam structure is monocyclic - a single beta-lactam ring standing alone. It was originally isolated from *Chromobacterium violaceum*. [1]
2. Its activity is concentrated on aerobic gram-negative bacilli, and it is resistant to many beta-lactamases. In practical terms its spectrum more closely resembles that of the aminoglycosides than that of the penicillins, which is a useful way to remember what it does and does not reach. [1]
3. The reason aztreonam still matters clinically, despite a narrow spectrum and an old registration, is a structural quirk: class B metallo-beta-lactamases hydrolyse every beta-lactam except this one. When an organism produces NDM, IMP or VIM, aztreonam is the beta-lactam still standing. [4]

Classification and drug examples

Intro: A single-agent class in practice. Rather than subdividing by spectrum, the useful split is by route, because the inhalational formulation exists for a different purpose from the systemic one.

1. Name: Systemic monobactam

1. Note: Given intravenously or intramuscularly for systemic gram-negative infection.

Name: Aztreonam

Azactam

Route: IV/IM

Note: Used for moderate-to-severe systemic, skin, intra-abdominal, genitourinary and respiratory gram-negative infections. [1] [1]

2. Name: Inhalational monobactam

2. Note: A separate inhaled formulation delivering the same molecule to the airway.

Name: Aztreonam for inhalation

Cayston

Route: Inhalation

Note: An inhalational formulation of aztreonam. [1] [1]

Mechanism of action

Summary: Aztreonam binds penicillin-binding proteins, inhibiting cell-wall synthesis and decreasing bacterial growth - the standard beta-lactam mechanism delivered by a monocyclic ring.

Target: Penicillin-binding proteins (bacterial transpeptidases)

Cidal Static: bactericidal

Kill Kinetics: time-dependent

1. Step: 1

1. Title: A single beta-lactam ring reaches the target

1. Detail: The monocyclic beta-lactam structure is what distinguishes monobactams from the fused-ring penicillins, cephalosporins and carbapenems, which all acylate the same transpeptidases from a two-ring scaffold. [1][5]

2. Step: 2

2. Title: It binds penicillin-binding proteins

2. Detail: Aztreonam binds penicillin-binding proteins, the transpeptidases that cross-link peptidoglycan. [1]

3. Step: 3

3. Title: Cell-wall synthesis is inhibited

3. Detail: Inhibiting those enzymes prevents cell-wall synthesis and decreases bacterial growth. [1]

4. Step: 4

4. Title: The structure also explains its survival

4. Detail: The same monocyclic structure is why class B metallo-beta-lactamases, which hydrolyse all other beta-lactams, cannot hydrolyse aztreonam. [4]

Spectrum of activity

Intro: Narrow and gram-negative. Learning what aztreonam does not cover matters as much as learning what it does.

Subclass Id: systemic

Aerobic gram-negative bacilli

1. Gram-positive organisms

2. Anaerobes [1]

Major clinical uses

1. Drug: Aztreonam

1. Organism: Aerobic gram-negative bacilli

1. Indication: Moderate-to-severe systemic gram-negative infection

1. Line: targeted

1. Note: Chosen when gram-negative cover is needed and the organism is susceptible. [1]

2. Drug: Aztreonam

2. Organism: Aerobic gram-negative bacilli

2. Indication: Intra-abdominal infection

2. Line: targeted

2. Note: Gram-negative component only; anaerobic cover must come from elsewhere. [1]

3. Drug: Aztreonam

- 3. Organism: Aerobic gram-negative bacilli
- 3. Indication: Genitourinary infection
- 3. Line: targeted
- 3. Note: One of the licensed gram-negative indications. [1]
- 4. Drug: Aztreonam
- 4. Organism: Aerobic gram-negative bacilli
- 4. Indication: Skin and respiratory gram-negative infection
- 4. Line: targeted
- 4. Note: An inhalational formulation exists for airway delivery. [1]
- 5. Drug: Aztreonam
- 5. Organism: Metallo-beta-lactamase producers (NDM, IMP, VIM)
- 5. Indication: Infection where all other beta-lactams are hydrolysed
- 5. Line: reserve
- 5. Note: Class B enzymes hydrolyse every beta-lactam except aztreonam, which is what creates this niche. [4]

Pharmacokinetics

- 1. Drug: Aztreonam
- 1. Route: IV/IM
- 1. Absorption: Parenteral administration required
- 1. Csf Penetration: See prescribing reference
- 1. Metabolism: See prescribing reference
- 1. Elimination: See prescribing reference
- 1. Half Life: See prescribing reference
- 1. Dose Adjust: See prescribing reference [1]
- 2. Drug: Aztreonam for inhalation
- 2. Route: Inhalation
- 2. Absorption: Delivered directly to the airway
- 2. Csf Penetration: Not applicable
- 2. Metabolism: See prescribing reference
- 2. Elimination: See prescribing reference
- 2. Half Life: See prescribing reference
- 2. Dose Adjust: See prescribing reference [1]
- 1. Because only one molecule represents this class, its handling in the body is best read directly from a current prescribing reference rather than generalised as a class property. [1]
- 2. This page gives no dose regimens by design. Doses depend on indication, organism, renal function, age and weight, and belong in a prescribing reference used by the treating clinician.

Adverse effects

- 1. Effect: Injection site phlebitis
- 1. Detail: A common consequence of intravenous administration. [1]
- 2. Effect: Rash
- 2. Detail: Reported as a common side effect. [1]
- 3. Effect: Gastrointestinal symptoms
- 3. Detail: Reported as a common side effect. [1]
- 1. Effect: Liver enzyme elevation
- 1. Detail: Asymptomatic elevations occur in roughly 10 to 38% of patients receiving high-dose intravenous therapy, though these are typically mild and self-limited.

1. Action: Interpret alongside the clinical picture; seek assessment if symptomatic liver disease develops. [1]
2. Effect: Hypersensitivity reactions, including anaphylaxis and angioedema
2. Detail: Cross-reactivity with other beta-lactams is rare, which is the basis of aztreonam's role in penicillin allergy. The exception is ceftazidime: the two share a structurally identical side chain, so a specifically ceftazidime-directed allergy warrants added caution.
2. Action: An allergy history is taken before administration; the drug is stopped and the reaction treated if one occurs. [2][3]
3. Effect: Toxic epidermal necrolysis
3. Detail: Reported with aztreonam, described in bone marrow transplant recipients carrying multiple concurrent risk factors.
3. Action: The drug is stopped if a serious skin reaction develops. [2]

Contraindications, precautions and interactions

1. Known hypersensitivity to aztreonam. Allergy history should always be established before any beta-lactam is given. [1]
2. Reliance on aztreonam for cover it does not provide. Because its activity is confined to aerobic gram-negative bacilli, gram-positive and anaerobic cover must come from another agent when both are needed. [1]

Resistance mechanisms

1. Mechanism: Class A serine carbapenemases
 1. Detail: These enzymes hydrolyse penicillins, cephalosporins, carbapenems and aztreonam, so they defeat aztreonam along with everything else.
KPC
 1. Countermeasure: Newer inhibitor combinations, directed by susceptibility testing. [4]
 2. Mechanism: Class B metallo-beta-lactamases - the exception
 2. Detail: Zinc-dependent enzymes that hydrolyse all beta-lactams except aztreonam. This is why aztreonam retains a role against these organisms rather than losing one.
 1. NDM
 2. IMP
 3. VIM
 2. Countermeasure: Aztreonam itself, often paired with an agent that neutralises any co-produced serine enzyme. [4]
 3. Mechanism: Porin loss and efflux
 3. Detail: Reduced permeability and active export limit how much drug reaches penicillin-binding proteins, independent of any enzyme.
 3. Countermeasure: Susceptibility-directed therapy. [4]
- Stewardship Note: Aztreonam's value is highly situational: it is unremarkable as general gram-negative cover and genuinely important against metallo-beta-lactamase producers. Susceptibility testing is what tells those two situations apart.

High-yield exam pearls

1. Pearl: Metallo-beta-lactamases spare aztreonam.
1. Why: Class B carbapenemases hydrolyse every beta-lactam except aztreonam, which is what makes it a therapeutic option against NDM, IMP and VIM producers. [4]
2. Pearl: Aztreonam behaves more like an aminoglycoside than a penicillin in terms of what it covers.
2. Why: Its activity is concentrated on aerobic gram-negative bacilli rather than the gram-positive and anaerobic range a penicillin reaches. [1]

3. Pearl: The exception does not extend to serine carbapenemases.
3. Why: Class A enzymes including KPC hydrolyse penicillins, cephalosporins, carbapenems and aztreonam alike. [4]
4. Pearl: There is effectively one monobactam to learn.
4. Why: Aztreonam is the agent that represents this class in practice, so the class and the drug are studied together. [1]

Common exam traps

1. Trap: "Aztreonam resists all beta-lactamases."
1. Correction: It is resistant to many beta-lactamases and specifically survives class B metallo-enzymes, but class A carbapenemases such as KPC hydrolyse it. [1][4]
2. Trap: "Monobactams are broad-spectrum like carbapenems."
2. Correction: Aztreonam is active mostly against gram-negative organisms, specifically aerobic gram-negative bacilli - a much narrower profile than a carbapenem. [1]
3. Trap: "Aztreonam can be given orally for gram-negative cover."
3. Correction: It is administered parenterally, by intravenous or intramuscular injection, with an inhalational formulation available for a specific respiratory use. [1]

Self-test questions

1. Question: Which structural feature distinguishes a monobactam from the other beta-lactam classes?
 1. A beta-lactam ring fused to a thiazolidine ring
 2. Two beta-lactam rings joined in series
 3. No beta-lactam ring at all
 4. A single, monocyclic beta-lactam ring that is not fused to a second ring
1. Explanation: Penicillins, cephalosporins and carbapenems all present their beta-lactam ring attached to a second ring; the monobactam scaffold carries just the one. Aztreonam, the agent that represents this class in practice, was originally obtained from *Chromobacterium violaceum*. [1]
2. Question: How does aztreonam exert its antibacterial effect?
 1. It binds penicillin-binding proteins, so cell-wall synthesis is inhibited and bacterial growth falls
 2. It binds the 30S ribosomal subunit and causes misreading of the genetic code
 3. It binds the D-alanyl-D-alanine terminus of the peptidoglycan precursor
 4. It inhibits DNA gyrase and prevents supercoiling
2. Explanation: Despite its unusual single-ring scaffold, aztreonam works in the conventional beta-lactam way. It attaches to the transpeptidases that cross-link peptidoglycan, and once wall construction is blocked the organism's growth declines. [1]
3. Question: Aztreonam is selected to cover the gram-negative component of an intra-abdominal infection. Which organisms does it leave uncovered?
 1. Aerobic gram-negative bacilli
 2. Enterobacterales that produce no beta-lactamase
 3. Gram-positive organisms and anaerobes
 4. Only organisms producing metallo-beta-lactamases
3. Explanation: This drug's reach stops at aerobic gram-negative bacilli, which is a much narrower profile than a carbapenem offers. Anything gram-positive and anything anaerobic requires a second agent, so relying on aztreonam alone in a mixed abdominal picture leaves a gap. [1]
4. Question: Which enzyme group hydrolyses every beta-lactam except aztreonam?
 1. Class A serine carbapenemases such as KPC
 2. Class B metallo-beta-lactamases such as NDM, IMP and VIM
 3. Mutationally altered penicillin-binding proteins
 4. Efflux pumps acting together with porin loss

4. Explanation: The zinc-dependent class B enzymes dismantle the entire beta-lactam family with a single exception, and that exception is aztreonam. It is the whole reason a narrow, elderly agent still earns a place when NDM, IMP or VIM is present. [4]

5. Question: Why is the statement "aztreonam resists all beta-lactamases" incorrect?

1. Metallo-beta-lactamases hydrolyse it more efficiently than they hydrolyse carbapenems

2. Porin loss is itself a form of enzymatic hydrolysis

3. Class A serine carbapenemases, KPC among them, hydrolyse aztreonam as readily as penicillins, cephalosporins and carbapenems

4. Aztreonam contains no beta-lactam ring for any enzyme to attack

5. Explanation: The drug does survive many beta-lactamases and specifically escapes the class B enzymes, but that immunity is not general. Serine carbapenemases of class A take it apart just as they take apart the fused-ring agents, so the exception applies to one enzyme class only. [1][4]

6. Question: By which route or routes is aztreonam administered?

1. Orally only

2. Parenterally, by intravenous or intramuscular injection, with an inhalational formulation also available

3. Orally, with injection reserved for severe infection

4. By inhalation only

6. Explanation: Systemic therapy with this molecule means injection, either into a vein or into muscle. A separate inhaled preparation delivers the same drug straight to the airway, so two routes exist and neither of them is swallowing a tablet. [1]

Frequently asked questions

1. Question: What makes a monobactam different from a penicillin?

1. Answer: Structure. A monobactam has a monocyclic beta-lactam ring standing alone, whereas penicillins, cephalosporins and carbapenems carry a beta-lactam ring fused to a second ring. Aztreonam is the monobactam used in practice. [1]

2. Question: Why is aztreonam useful against NDM-producing organisms?

2. Answer: Class B metallo-beta-lactamases, of which NDM is one, hydrolyse all beta-lactams except aztreonam. That single exception is what keeps it usable when every other beta-lactam has been inactivated. [4]

3. Question: Does aztreonam cover gram-positive organisms or anaerobes?

3. Answer: No. Its activity is directed mostly at gram-negative organisms, specifically aerobic gram-negative bacilli. Cover for gram-positives or anaerobes has to come from another agent. [1]

4. Question: How is aztreonam given?

4. Answer: Parenterally, by intravenous or intramuscular injection. An inhalational formulation is also available. [1]

References

[1] Aztreonam (LiverTox). LiverTox, NIDDK / NCBI Bookshelf 2020. <https://www.ncbi.nlm.nih.gov/books/NBK548462/>

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[4] Carbapenem-Resistant Enterobacterales (StatPearls). StatPearls Publishing / NCBI Bookshelf 2024. <https://www.ncbi.nlm.nih.gov/books/NBK551704/>

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