Azlocillin Sodium *(BANM, rINNM)*

Azlocilina sódica; Azlocilline Sodique; Azlocillinum Natricum; Azlocylina sodowa; Bay-e-6905; Natrii Azlocillinum. Sodium (6*R*)-6-[D-2-(2-oxoimidazolidine-1-carboxamido)-2-phenylacetamido]penicillanate.

Натрий Азлоциллин

$C_{20}H_{22}N_5NaO_6S$ = 483.5.

CAS — 37091-65-9.

ATC — J01CA09.

ATC Vet — QJ01CA09.

Pharmacopoeias. In *Pol.*

Incompatibility. Azlocillin sodium has been reported to be incompatible with aminoglycosides, ciprofloxacin, metronidazole, and tetracyclines.

Adverse Effects and Precautions

As for Carbenicillin Sodium, p.216.

Prolongation of bleeding time has been less frequent and less severe with azlocillin than with carbenicillin.

Hypouricaemia. Reports of transient asymptomatic decreases in serum-uric acid concentrations during treatment with azlocillin.[1,2]

1. Faris HM, Potts DW. Azlocillin and serum uric acid. *Ann Intern Med* 1983; **98:** 414.
2. Ernst JA, Sy ER. Effect of azlocillin on uric acid levels in serum. *Antimicrob Agents Chemother* 1983; **24:** 609–10.

Sodium content. Each g of azlocillin sodium contains about 2.1 mmol of sodium. As azlocillin sodium has a lower sodium content than carbenicillin sodium, hypernatraemia and hypokalaemia are less likely to occur.

Interactions

As for Benzylpenicillin, p.214.

Antibacterials. For the effect of azlocillin on the clearance of *cefotaxime*, and a report of neurotoxicity, see p.228. For reference to azlocillin affecting the disposition of *ciprofloxacin*, see p.246.

Antimicrobial Action

Azlocillin has an antimicrobial action similar to that of piperacillin (p.315). Its activity *in vitro* against Enterobacteriaceae is generally less than that of mezlocillin or piperacillin, but it has comparable activity to piperacillin against *Pseudomonas aeruginosa*.

Pharmacokinetics

Azlocillin is not absorbed from the gastrointestinal tract to any significant extent. It has nonlinear dose-dependent pharmacokinetics. Doubling an intravenous dose results in more than double the plasma concentration. Between 20 and 46% of azlocillin in the circulation is bound to plasma proteins. The plasma half-life is usually about 1 hour, but is longer in neonates; in patients with renal impairment half-lives of 2 to 6 hours have been reported.

Azlocillin is widely distributed in body tissues and fluids. It crosses the placenta into the fetal circulation and small amounts are distributed into breast milk. There is little diffusion into the CSF except when the meninges are inflamed.

Azlocillin is metabolised to a limited extent. About 50 to 70% of a dose is excreted unchanged in the urine by glomerular filtration and tubular secretion within 24 hours of a dose, resulting in high urinary concentrations. Azlocillin is partly excreted in the bile where it is also found in high concentrations.

Plasma concentrations are enhanced if probenecid is given.

Azlocillin is removed by haemodialysis.

Uses and Administration

Azlocillin is a ureidopenicillin and, like piperacillin (p.316), is used mainly for the treatment of infections caused by *Pseudomonas aeruginosa*. It has been used particularly for septicaemia, and infections of the respiratory and urinary tracts, and also for peritonitis; for details of these infections, see under Choice of Antibacterial, p.162.

Azlocillin is commonly used with an aminoglycoside; however, they should be given separately as they have been shown to be incompatible (see Incompatibility, above).

Administration and dosage. Azlocillin is given intravenously as the sodium salt. Doses are expressed in terms of the equivalent amount of azlocillin; 1.05 g of azlocillin sodium is equivalent to about 1 g of azlocillin. A 10% solution in a suitable diluent is given by slow injection for doses of 2 g or less; higher doses should be infused over 20 to 30 minutes.

The usual adult dose is 5 g every 8 hours for life-threatening infections, or 2 g every 8 hours for less severe infections and urinary-tract infections.

The following doses may be used for children: premature infants, 50 mg/kg twice daily; neonates less than 7 days old, 100 mg/kg twice daily; infants between 7 days and 1 year, 100 mg/kg three times daily; children up to 14 years, 75 mg/kg three times daily.

Dosage of azlocillin may need to be adjusted in patients with hepatic or renal impairment (see below).

Administration in hepatic or renal impairment. The interval between doses of azlocillin may need to be increased to every 12 hours in moderate to severe renal impairment (creatinine clearance less than 30 mL/minute); additional dosage reductions may be needed in patients with both severe renal and hepatic impairment.

Aztreonam *(BAN, USAN, rINN)*

Atstreonaami; Azthreonam; Aztréonam; Aztreonamum; SQ-26776. (*Z*)-2-{2-Aminothiazol-4-yl-[(2*S*,3*S*)-2-methyl-4-oxo-1-sulphoazetidin-3-ylcarbamoyl]methyleneamino-oxy}-2-methylpropionic acid.

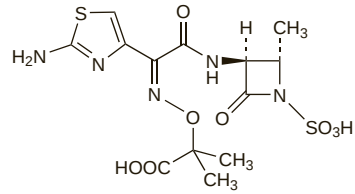
Азтреонам

$C_{13}H_{17}N_5O_8S_2$ = 435.4.

CAS — 78110-38-0.

ATC — J01DF01.

ATC Vet — QJ01DF01.



Pharmacopoeias. In *Jpn* and *US*, which allows the anhydrous or hydrated forms.

USP 31 (Aztreonam). A white, odourless crystalline powder. Very slightly soluble in dehydrated alcohol; practically insoluble in chloroform, in ethyl acetate, and in toluene; soluble in dimethylformamide and in dimethyl sulfoxide; slightly soluble in methyl alcohol. Store in airtight containers.

Incompatibility and stability. Aztreonam has been reported to be incompatible with cefradine, metronidazole, nafcillin, and vancomycin.

References.

1. Bell RG, *et al.* Stability of intravenous admixtures of aztreonam and cefoxitin, gentamicin, metronidazole, or tobramycin. *Am J Hosp Pharm* 1986; **43:** 1444–53.
2. Riley CM, Lipford LC. Interaction of aztreonam with nafcillin in intravenous admixtures. *Am J Hosp Pharm* 1986; **43:** 2221–4.
3. Belliveau PP, *et al.* Stability of aztreonam and ampicillin sodium-sulbactam sodium in 0.9% sodium chloride injection. *Am J Hosp Pharm* 1994; **51:** 901–4.
4. Trissel LA, Martinez JF. Compatibility of aztreonam with selected drugs during simulated Y-site administration. *Am J Health-Syst Pharm* 1995; **52:** 1086–90.
5. Trissel LA, *et al.* Compatibility and stability of aztreonam and vancomycin hydrochloride. *Am J Health-Syst Pharm* 1995; **52:** 2560–4.

Adverse Effects

The adverse effects of aztreonam are similar to those of other beta lactams (see Benzylpenicillin, p.213, and Cefalotin, p.219). Hypersensitivity reactions, including skin rashes, urticaria, angioedema, exfoliative dermatitis, eosinophilia, bronchospasm, and rarely anaphylaxis and toxic epidermal necrolysis, may occur in patients receiving aztreonam, although it has been reported to be only weakly immunogenic. Gastrointestinal effects include diarrhoea, nausea, vomiting, mouth ulcer, and an abnormal taste.

Phlebitis or thrombophlebitis has been reported after the intravenous use of aztreonam, and pain or swelling after intramuscular injection.

Use of aztreonam may result in the overgrowth of non-susceptible organisms, including Gram-positive cocci. Pseudomembranous colitis or gastrointestinal bleeding may develop.

Other adverse effects that have been reported with aztreonam include jaundice and hepatitis, increases in liver enzymes, and prolongation of prothrombin and partial thromboplastin times.

Effects on the skin. References.

1. McDonald BJ, *et al.* Toxic epidermal necrolysis possibly linked to aztreonam in bone marrow transplant patients. *Ann Pharmacother* 1992; **26:** 34–5.

Precautions

Aztreonam should not be given to patients who are hypersensitive to it and should be used with caution in those known to be hypersensitive to other beta lactams, although the incidence of cross-sensitivity appears to be low (but see below).

Aztreonam should be used with caution in patients with renal or hepatic impairment.

Breast feeding. In a study in 12 healthy women given aztreonam, peak concentrations in breast milk were found to be less than 1% of those in serum and this was considered suggestive of a low risk of adverse effects in breast-fed infants.[1] The American Academy of Pediatrics states that no adverse effects have been seen in breast-fed infants whose mothers received aztreonam and considers it to be usually compatible with breast feeding,[2] although UK licensed product information recommends that mothers should refrain from breast feeding while receiving aztreonam.

1. Fleiss PM, *et al.* Aztreonam in human serum and breast milk. *Br J Clin Pharmacol* 1985; **19:** 509–11.
2. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 25/05/04)

Hypersensitivity. Aztreonam is said to show little cross-reactivity with other beta lactams,[1,2] but there have been isolated reports of immediate hypersensitivity to aztreonam in patients with a history of hypersensitivity to penicillin.[3,4]

1. Saxon A, *et al.* Lack of cross-reactivity between aztreonam, a monobactam antibiotic, and penicillin in penicillin-allergic subjects. *J Infect Dis* 1984; **149:** 16–22.
2. Adkinson NF. Immunogenicity and cross-allergenicity of aztreonam. *Am J Med* 1990; **88** (suppl 3C): 12S–15S.
3. Alvarez JS, *et al.* Immediate hypersensitivity to aztreonam. *Lancet* 1990; **335:** 1094.
4. Hantson P, *et al.* Immediate hypersensitivity to aztreonam and imipenem. *BMJ* 1991; **302:** 294–5.

Interactions

Caution is recommended in patients receiving aztreonam and oral anticoagulants because of the possibility of increased prothrombin time.

Antimicrobial Action

Aztreonam is bactericidal and acts similarly to the penicillins by inhibiting synthesis of the bacterial cell wall; it has a high affinity for the penicillin-binding protein 3 (PBP-3) of Gram-negative bacteria. The activity of aztreonam is restricted to Gram-negative aerobic organisms, including beta-lactamase-producing strains, with poor or no activity against Gram-positive aerobes or anaerobic organisms. It is active against most Enterobacteriaceae including *Escherichia coli*, *Klebsiella*, *Proteus*, *Providencia*, *Salmonella*, *Serratia*, *Shigella*, and *Yersinia* spp. Some strains of *Enterobacter* and *Citrobacter* spp. are resistant. Aztreonam has some activity against *Pseudomonas aeruginosa*, although most strains of other *Pseudomonas* spp. are insensitive. Aztreonam has good activity against *Haemophilus influenzae* and *Neisseria* spp.

Synergy has been reported *in vitro* between aztreonam and aminoglycosides against *Ps. aeruginosa* and some *Enterobacteriaceae*.

Aztreonam is stable to hydrolysis by many beta-lactamases and appears to be a poor inducer of beta-lactamase production. Acquired resistance has occasionally been reported.

Pharmacokinetics

Aztreonam is poorly absorbed from the gastrointestinal tract and is therefore given parenterally. Absorption after intramuscular injection is good; peak plasma concentrations of about 46 micrograms/mL have been achieved within 1 hour of a 1-g dose. Aztreonam has a plasma half-life of about 1.7 hours. The half-life may be prolonged in neonates, in the elderly, in patients with renal impairment, and to some extent in those with hepatic impairment. Aztreonam is about 56% bound to plasma proteins. It is widely distributed in body tissues and fluids, including bile. Diffusion into the CSF is poor unless the meninges are inflamed. It crosses the placenta and enters the fetal circulation; small amounts are distributed into breast milk.

Aztreonam is not extensively metabolised. The principal metabolite, SQ-26992, is inactive and is formed by opening of the beta-lactam ring; it has a much longer half-life than the parent compound. Aztreonam is excreted mainly in the urine, by renal tubular secretion