

Size : 240x110mm

60gsm without fold

Immune system disorders	Not Known	Anaphylactic reaction
Investigations	Rare	Electrocardiogram change
Musculoskeletal, connective tissue and bone disorders	Rare	Myalgia
Nervous system disorders	Rare	Convulsions ^a , paraesthesia, dizziness, headache
	Not Known	Dysgeusia Encephalopathy (confusional state, altered state of consciousness, epilepsy, movement disorder)
Psychiatric disorders	Rare	Confusional state, insomnia
Renal and urinary disorders	Uncommon	Blood creatinine increased
Reproductive system and breast disorders	Rare	Breast tenderness
Respiratory, thoracic and mediastinal disorders	Rare	Wheezing, dyspnoea, sneezing, nasal congestion
	Not Known	Bronchospasm
Skin and subcutaneous tissue disorders		Toxic epidermal necrolysis ^a , angioedema, erythema multiforme, dermatitis exfoliative, hyperhidrosis, petechiae, purpura, urticaria, rash, pruritus
Vascular disorders	Rare	Hypotension, haemorrhage
	Not Known	Phlebitis, thrombophlebitis, flushing

^aUsually reversing during therapy and without overt signs or symptoms of hepatobiliary dysfunction.

Overdose
Use of beta-lactam containing therapies, including aztreonam, can cause encephalopathy (e.g. confusion, impairment of consciousness, epilepsy, movement disorders); particularly in patients with renal impairment and in association with beta-lactam overdose.
There have been no reported cases of overdose. If necessary, aztreonam may be cleared from the serum by hemodialysis and/or peritoneal dialysis. Aztreonam has been shown to be cleared from the serum by continuous arteriovenous hemofiltration.

Pharmacological Properties
Pharmacodynamic Properties: Pharmacotherapeutic group: Anti-infectives for systemic use, ATC code: J01DF01
Aztreonam is a monocyclic beta-lactam antibiotic with potent bactericidal activity against a wide spectrum of Gram negative aerobic pathogens. Unlike the majority of beta-lactam antibiotics, it is not an inducer in vitro of beta-lactamase activity. Aztreonam is usually active in vitro against those resistant aerobic organisms whose beta-lactamases hydrolyse other antibiotics.
Pharmacokinetic Properties: Single 30-minute i.v. infusions of 0.5 g, 1.0 g and 2.0 g in healthy volunteers produced peak serum levels of 54, 90 and 204

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mg/L and single 3-minute i.v. injections of the same doses produced peak levels of 58, 125 and 242 mg/L. Peak levels of aztreonam are achieved at about one hour after i.m. administration. After identical single i.m. or i.v. doses, the serum concentrations are comparable at 1 hour (1.5 hours from the start of i.v. infusion), with similar slopes of serum concentrations thereafter.
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 i.m. or i.v. dose was recovered in the urine by 8 hours, and urinary excretion was essentially complete by 12 hours.
Preclinical safety data: Aztreonam was well tolerated in a comprehensive series of preclinical toxicity and safety studies.

Pharmaceutical Properties
List of excipients: L-arginine

Incompatibilities
Aztreonam should not be physically mixed with any other drug, antibiotic or diluent, except those listed in the Posology and Method of Administration section under Reconstitution for Intravenous infusion.
With intermittent infusion of Aztreonam and another drug via a common delivery tube, the 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.

Special precautions for storage
a) Product unopened:
Storage before reconstitution: Store below 30°C. Protect from light.
b) Reconstituted product:
Stability after reconstitution: Store at 2-8°C for not more than 18 hours. Discard any unused solution.

Nature and contents of container
20 mL clear glass vials, closed with 20 mm rubber plug and 20 mm flip off seal.

Special precautions for disposal and other handling
Reconstitution: Aztreonam is supplied in 20 mL vials.
Upon the addition of the diluent the contents should be shaken immediately and vigorously. Vials of reconstituted Aztreonam are not intended for multi-dose use, and any unused solution from a single dose must be discarded.
Depending on the type and amount of diluent, the pH ranges from 4.5 to 7.5 and the colour may vary from colourless to light straw-yellow, which may develop a slight pink tint on standing; however this does not affect the potency.
For intramuscular injection: For each gram of aztreonam add at least 3 mL Water for Injections or 0.9% Sodium Chloride Injection and shake well.
For intravenous injection: To the contents of the vial add 6 to 10 mL of Water for Injections and shake well. Slowly inject directly into the vein over a period of 3 to 5 minutes.

Single Dose Vial Size	Volume of Diluent to be Added
1.0 g	3.0 mL

For intravenous infusion:
Vials: For each gram of aztreonam add at least 3 mL of Water for Injections and

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shake well.
Dilute this initial solution with an appropriate infusion solution to a final concentration less than 2% w/v (at least 50 mL solution per gram of aztreonam). The infusion should be administered over 20-60 minutes.
Appropriate infusion solutions include: 0.9% Sodium Chloride Injection, 5% Glucose Intravenous Infusion, 5% or 10% Mannitol Intravenous Infusion, Sodium Lactate Intravenous Infusion, 0.9% Sodium Chloride and 5% Glucose Intravenous Infusion
A volume control administration set may be used to deliver the initial solution of Aztreonam into a compatible infusion solution being administered. With use of a Y-tube administration set, careful attention should be given to the calculated volume of Aztreonam solution required so that the entire dose will be infused.
If aztreonam and metronidazole are to be used together, they should be administered separately as a cherry red colour has been observed after storage of solutions containing combinations of the two products.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

For Suspected Adverse Drug Reaction, report to the FDA: www.fda.gov.ph and BIOCARE: pv@biocarelifesciences.com
Seek medical attention immediately at the first sign of any adverse drug reaction.

CAUTION: Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

FDA Reg. No.: DRP-17465

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1 Vial

Aztreonam
MONOBAC
1 gram Powder for Injection (IM/IV)
Antibacterial



Name of the Medicinal Product
Aztreonam 1 gram Powder for Injection (IM/IV)

Qualitative and Quantitative Composition
Each vial contains:
Aztreonam USP
Equivalent to Anhydrous Aztreonam 1.0 g
(Aztreonam is a sterile, dry mixture of Aztreonam and L-arginine. The L-Arginine at an approximate 780 mg/g of Aztreonam is added to control the pH of constituted solution at 4.5 to 7.5)

Pharmaceutical Form: Powder for Solution for Injection or Infusion
Aztreonam is a white odorless crystalline powder, free from extraneous particles, contained in colorless glass vials.

Clinical Particulars
Therapeutic Indications: The treatment of the following infections caused by susceptible aerobic Gram-negative micro-organisms:
Urinary tract infections: including pyelonephritis and cystitis (initial and recurrent) and asymptomatic bacteriuria, including those due to pathogens resistant to the aminoglycosides, cephalosporins or penicillins.
Gonorrhoea: acute uncomplicated urethral or anorectal infections due to beta-lactamase producing or non-producing strains of N. gonorrhoeae.
Lower respiratory tract infections: including pneumonia, bronchitis and lung infections in patients with cystic fibrosis.
Bacteraemia/septicemia.
Meningitis caused by Haemophilus influenzae or Neisseria meningitidis.
Since Aztreonam provides only Gram negative cover, it should not be given alone as initial blind therapy, but may be used with an antibiotic active against Gram positive organisms until the results of sensitivity tests are known.
Bone and joint infections.
Skin and soft tissue infections: including those associated with postoperative wounds, ulcers and burns.
Intra-abdominal infections: peritonitis.
Gynaecological infections: pelvic inflammatory disease, endometritis and pelvic cellulitis.
Aztreonam is indicated for adjunctive therapy to surgery in the management of infections caused by susceptible organisms, including abscesses, infections

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complicating hollow viscus perforations, cutaneous infections and infections of serous surfaces.
Bacteriological studies to determine the causative organism(s) and their sensitivity to aztreonam should be performed.
Therapy may be instituted prior to receiving the results of sensitivity tests. In patients at risk of infections due to non-susceptible pathogens, additional antibiotic therapy should be initiated concurrently with Aztreonam to provide broad-spectrum coverage before identification and susceptibility testing results of the causative organism(s) are known. Based on these results, appropriate antibiotic therapy should be continued.
Patients with serious Pseudomonas infections may benefit from concurrent use of Aztreonam and an aminoglycoside because of their synergistic action. If such concurrent therapy is considered in these patients, susceptibility tests should be performed in vitro to determine the activity in combination. The usual monitoring of serum levels and renal function during aminoglycoside therapy applies.

Posology and method of administration
Posology: Intramuscular or intravenous injection, or intravenous infusion. Aztreonam is given by deep injection into a large muscle mass, such as the upper quadrant of the gluteus maximus or the lateral part of the thigh.
Adults: The dose range of Aztreonam is 1 to 8 g daily in equally divided doses. The usual dose is 3 to 4 g daily. The maximum recommended dose is 8 g 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.
Dosage Guide: Adults (see table below)

Type of infection ¹	Dosage	Frequency (hours)	Route
Urinary Tract Infections	500 mg or 1 g	8 or 12	IM or IV
Gonorrhoea / cystitis	1 g	Single Dose	IM
Cystic fibrosis	2 g	6 - 8	IV
Moderately severe systemic infections	1 g or 2 g	8 or 12	IM or IV
Severe systemic or life-threatening infections	2 g	6 or 8	IM or IV
Other infections either or	1 g	8	IM or IV
	2 g	12	IV

¹ Because of the serious nature of infections due to *Pseudomonas aeruginosa*, a dose of 2 g every 6 or 8 hours is recommended, at least for initial 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, localised parenchymal abscess (e.g. intra-abdominal abscess), peritonitis, meningitis or other severe systemic or life-threatening infections.
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. Elderly patients normally have a creatinine clearance in excess of 30 mL/min

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and therefore would receive the normal recommended dose. If renal function is below this level, the dosage schedule should be adjusted (see Renal Impairment).
Renal Impairment: Prolonged serum levels of aztreonam may occur in patients with transient or persistent renal insufficiency. Therefore, after an initial usual dose, the dosage of aztreonam should be halved in patients with estimated creatinine clearances between 10 and 30 mL/min/1.73 m.
In patients with severe renal failure (creatinine clearance less than 10 mL/min/1.73 m), such as those supported by hemodialysis, the usual dose 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.
Hepatic impairment: A dose reduction of 20-25% is recommended for long-term treatment of patients with chronic liver disease with cirrhosis, especially in cases of alcoholic cirrhosis and when renal function is also impaired.
Paediatric population: 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. The recommended dose for all patients in the treatment of infections due to P. aeruginosa is 50 mg/kg every six to eight hours.
The maximum daily paediatric dose should not exceed the maximum recommended dose for adults.
Dosage information is not yet available for new-borns less than 1 week old.
Method of administration: For instructions on dilution of the product before administration, see section Special precautions for disposal and other handling.

Contraindications
Hypersensitivity to the active substance(s) or to any of the excipients listed in list of excipients.
Aztreonam is contraindicated in pregnancy. Aztreonam crosses the placenta and enters the foetal circulation.

Special warnings and precautions for use
Allergic reactions: Antibiotics, like other drugs, should be given with caution to any patients with a history of allergic reaction to structurally related compounds. If an allergic reaction occurs, discontinue the drug and institute supportive treatments as appropriate. Serious hypersensitivity reactions may require epinephrine and other emergency measures. Specific studies have not shown significant cross-reactivity between Aztreonam and antibiotics to penicillins or cephalosporins. The incidence of hypersensitivity to Aztreonam in clinical trials has been low but caution should be exercised in patients with a history of hypersensitivity to beta-lactam antibiotics until further experience is gained.
Renal/hepatic impairment: As with some other beta-lactams there have been reports of encephalopathy with aztreonam (e.g. confusion, impairment of consciousness, epilepsy, movement disorders); particularly in patients with renal impairment and in association with beta-lactam overdose.
In patients with impaired hepatic or renal function, appropriate monitoring is recommended during therapy.
Serious blood/skin disorders: Serious blood disorders (incl. pancytopenia)

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and skin disorders (incl. toxic epidermal necrolysis) have been reported with the use of aztreonam. In case of serious hemogram and skin changes, it is recommended to stop aztreonam.
Convulsions: Convulsions have rarely been reported during treatment with beta-lactams, including aztreonam (see section Undesirable Effects).
Clostridium difficile associated diarrhoea: *Clostridium difficile* associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents, including Aztreonam, and may range in severity from mild diarrhoea to fatal colitis. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Medication that inhibits intestinal peristalsis should not be given.
Concurrent therapy with other antimicrobial agents and Aztreonam is recommended as initial therapy in patients who are at risk of having an infection due to pathogens that are not susceptible to aztreonam.
As with other antibiotics, in the treatment of acute pulmonary exacerbations in patients with cystic fibrosis, while clinical improvement is usually noted, lasting bacterial eradications may not be achieved.
Overgrowth of non-susceptible organisms: Therapy with Aztreonam may result in overgrowth of non-susceptible organisms, including gram-positive organisms and fungi. Should superinfection occur during therapy, appropriate measures should be taken. In comparative studies, the number of patients treated for superinfections was similar to that of the control drugs used.
Prolongation of prothrombin time / increased activity of oral anticoagulants: Prolongation of prothrombin time has been reported rarely in patients receiving aztreonam. Additionally, numerous cases of increased activity of oral anticoagulants have been reported in patients receiving antibiotics, including beta-lactams. Severe infection or inflammation, and the age and general condition of the patient appear to be risk factors. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.
Concomitant use with aminoglycosides: If an aminoglycoside is used concurrently with aztreonam, especially if high dosages of the former are used or if therapy is prolonged, renal function should be monitored because of the potential nephrotoxicity and ototoxicity of aminoglycoside antibiotics.
Paediatric population: Data on safety and effectiveness in neonates younger than one week are limited; use in this population needs to be carefully assessed.
Arginine: Aztreonam for injection contains arginine. Studies in low birth weight infants have demonstrated that arginine administered in the aztreonam formulation may result in increases in serum arginine, insulin, and indirect bilirubin. The consequences of exposure to this amino acid during treatment of neonates have not been fully ascertained.
Interference with serological testing: A positive direct or indirect Coombs test may develop during treatment with aztreonam.
Interactions with other medicinal products and other forms of interaction: Concomitant administration of probenecid or furosemide and aztreonam cause clinically insignificant increases in the serum levels of aztreonam.
Due to the induction of beta-lactamases, certain antibiotics (eg, cefoxitin,

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imipenem) have been found to cause antagonism with many beta-lactams, including aztreonam, for certain gram-negative aerobes, such as Enterobacter species and Pseudomonas species.
Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation (see section Special warnings and precautions for use and Undesirable effects).
Single-dose pharmacokinetic studies have not shown any significant interaction between aztreonam and gentamicin, cephadrine, clindamycin or metronidazole.
Unlike broad spectrum antibiotics, aztreonam produces no effects on the normal anaerobic intestinal flora. No disulfiram-like reactions with alcohol ingestion have been reported.

Fertility, pregnancy and lactation
Pregnancy: Aztreonam is contraindicated in pregnancy. Aztreonam crosses the placenta and enters the foetal circulation.
There are no adequate and well-controlled studies in pregnant women.
Breastfeeding: Aztreonam is excreted in breast milk in concentrations that are less than 1% of those in simultaneously obtained maternal serum. Lactating mothers should refrain from breast feeding during the course of therapy.
Effects on ability to drive and use machines: This medicine can have an important impact on the ability to drive and use of machines should encephalopathy occur.
Undesirable effects: The list of undesirable effects shown below is presented by system organ class, MedDRA preferred term and frequency. Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/100); rare (≥1/10,000 to <1/1000); very rare (≥1/10,000); Not known (cannot be estimated from the available data).

System Organ Class	Frequency	MedDRA Term
Blood and lymphatic system disorders	Rare	Pancytopenia ^a , thrombocytopenia, thrombocythaemia, leukocytosis, neutropenia, eosinophilia, anaemia, prothrombin time prolonged, activated partial thromboplastin time prolonged, Coombs test positive ^a
Ear and labyrinth disorders	Rare	Vertigo, tinnitus
Eye disorders	Rare	Diplopia
Gastrointestinal disorders	Rare	Gastro intestinal haemorrhage, <i>pseudomembranous colitis</i> , breath odour
	Not Known	Abdominal pains, mouth ulceration, nausea, vomiting, diarrhoea, altered taste
General disorders and administration site conditions	Rare	Chest pain, pyrexia, asthenia, malaise
	Not Known	Injection site discomfort, weakness, sweating, muscle aches, fever, transient increases in serum creatinine
Hepato-biliary disorders	Rare	Hepatitis, jaundice
	Not Known	Transaminases increased ^a , blood alkaline phosphatase increased ^a
Infections and infestations	Rare	Vaginitis, vaginal candidiasis

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