

DATA SHEET

IBIAMOX

Amoxycillin as 250mg, 500mg and 1000mg injections.

Presentation

Amoxycillin sodium equivalent to 250 mg, 500 mg and 1000 mg amoxycillin. White to cream powder packed in clear glass vials. Upon reconstitution the solutions may initially be red but rapidly become clear to pale yellow in colour.

Uses

Actions

IBIAMOX differs in-vitro from benzylpenicillin in the gram-negative spectrum. **IBIAMOX** has the same gram-positive and gram-negative spectrum as ampicillin.

In-vitro, most strains of Haemophilus influenzae, Neisseria gonorrhoea, Neisseria meningitidis, Escherichia coli, Proteus mirabilis and Salmonellae are sensitive to **IBIAMOX** at serum concentrations, which may be expected following the recommended doses.

Strains of gonococci which are relatively resistant to benzylpenicillin may be sensitive to **IBIAMOX**. In-vitro studies have also demonstrated the sensitivity of most strains of the following gram-positive bacteria: alpha- and beta-haemolytic streptococci, Streptococcus pneumoniae, non-penicillinase-producing staphylococci and Streptococcus faecalis.

However, some of the organisms were sensitive to **IBIAMOX** only at concentrations achieved in the urine.

IBIAMOX is not effective against penicillinase-producing bacteria, particularly resistant staphylococci.

All strains of Pseudomonas and most strains of Klebsiella and Aerobacter are resistant.

Like benzylpenicillin, **IBIAMOX** is bactericidal against sensitive organisms during the stage of active multiplication.

It is believed to act through the inhibition of biosynthesis of cell wall mucopeptide.

Pharmacokinetics

Amoxycillin is well absorbed after intra-muscular administration of any of the injection potencies, the relative bioavailability versus intravenous injection ranging from 73.2-96.7%.

IBIAMOX is widely distributed to most body tissues and fluids. It penetrates well into purulent and mucoid sputum and into the middle ear. Penetration into cells, the eye and the cerebral spinal fluid is poor. However, inflammation of the meninges increases the amount of amoxycillin that crosses the blood brain barrier.

About 75% of a 1g dose is excreted in the urine in 6 hours in the presence of normal renal function. 60% of this is unchanged and is excreted by glomerular filtration and tubular secretion. 15% is amoxycillin's metabolite, penicilloic acid.

The amount of **IBIAMOX** found in the bile is variable depending on normal biliary secretory function.

The half-life of **IBIAMOX** is 61.3 minutes with normal renal function. It is prolonged in neonates and the elderly due to incomplete or decreased renal function.

IBIAMOX is not highly protein-bound, being only 17% protein-bound in serum as compared to 59% for penicillin G.

Indications

Treatment of Infection: **IBIAMOX** is indicated in the treatment of infections due to susceptible strains of the following organisms.

Gram-negative organisms:	Gram-positive organisms:
Haemophilus influenzae	Streptococcus species
Escherichia coli	Streptococcus pneumoniae
Proteus mirabilis	Non-penicillinase-producing staphylococci
Neisseria gonorrhoea	

IBIAMOX may be useful in instituting therapy prior to bacteriology; however, bacteriological studies to determine the causative organisms and their sensitivity to **IBIAMOX** should be performed.

Prophylaxis of Endocarditis: **IBIAMOX** may be used for the prevention of bacteraemia, associated with procedures such as dental extraction, in patients at risk of developing bacterial endocarditis.

Dosage and Administration

Upper Respiratory Tract Infections: (Due to streptococci, pneumococci, non-penicillinase-producing staphylococci and H. influenzae)

Adults: 250mg every 8 hours.
Children: (under 20kg) 25mg/kg/day in equally divided doses every 8 hours.

Genito-Urinary Tract Infections: (Due to Escherichia coli, Proteus mirabilis and Strep. faecalis)

Adults: 250mg every 8 hours.
Children: (under 20kg) 25mg/kg/day in equally divided doses every 8 hours.

Skin and Soft Tissue Infections: (Due to Streptococci, sensitive Staphylococci and Escherichia coli)

Adults: 250mg every 8 hours.
Children: (under 20kg) 25mg/kg/day in equally divided doses every 8 hours.

In severe infections or those caused by less susceptible organisms, 500mg every 8 hours for adults and 50mg/kg/day in equally divided doses every 8 hours for children may be needed.

Lower Respiratory Tract Infections: (Due to Streptococci, Pneumococci, non-penicillinase-producing Staphylococci and Haemophilus influenzae).

Adults: 500mg every 8 hours.
Children: (under 20kg) 50mg/kg/day in equally divided doses every 12 hours.

Prophylaxis of Endocarditis - Dental Procedures: Prophylaxis for patients undergoing extraction, scaling or surgery involving gingival tissues who have not received a penicillin in the previous month.

Note: For patients fulfilling the criteria listed below, referral to hospital is recommended and oral antibiotics are considered inappropriate.

Patients to be given a general anaesthetic who have been given a penicillin in the previous month.

Patients to be given a general anaesthetic who have prosthetic heart valve.

Patients who have had one or more attacks of Endocarditis.

Appropriate parenteral therapy is:

Adults: Initially 1g **IBIAMOX I.M.** with 120mg gentamicin I.M. immediately prior to anaesthesia (if given) or 15 minutes prior to dental procedure.

Children: (under 10) The doses of **IBIAMOX** and **PENAMOX** should be half the adult dose; the dose of gentamicin should be 2mg/kg.

Consult the appropriate data sheet for full prescribing information on gentamicin. **IBIAMOX** and gentamicin should not be mixed in the same syringe.

Patients having a general anaesthetic in whom oral antibiotics are considered inappropriate should be treated with a parenteral antibiotic.

Adults: 1g **IBIAMOX I.M.** immediately before induction with 500mg **PENAMOX** orally 6 hours later.

Children: (under 10) Half adult dose.

Note: The childrens dose is intended for individuals whose weight will not cause dosage to be calculated greater than that recommended for adults.

Children weighing more than 20kg should be dosed according to the adult recommendations.

In renal impairment the excretion of the antibiotic will be delayed and, depending on the degree of impairment, it may be necessary to reduce the total daily dosage.

Treatment should be continued for a minimum of 48 to 72 hours beyond the time that the patient becomes asymptomatic or evidence of bacterial eradication has been obtained.

It is recommended that there be at least 10 days treatment for any infection caused by haemolytic streptococci to prevent the occurrence of rheumatic fever or glomerulonephritis.

Reconstitution of Vials: Solutions should be thoroughly mixed by vigorous shaking and checked for absence of particulate matter before use.

Routes of Administration:

1. Intramuscular Injection: Reconstitute with water for injections. Shake immediately after adding the diluent. Add 2mL to 250mg and 500mg vials and 4mL to 1g vial and inject the total volume produced.

A transient pink colouration or slight opalescence may appear during reconstitution. Reconstituted solutions are normally a pale straw colour.

If pain is experienced on intramuscular injection, a sterile 1% solution of lignocaine hydrochloride or 0.5% solution of procaine hydrochloride may be used in place of water for injections.

When giving part doses refer to the section on reconstitution of part doses.

2. Intravenous Injection: Reconstitute with 5mL of water for injections and shake immediately after adding the diluent.

Directly into infusion tubing: By slow injection (over 3-4 minutes) into the injection site of the giving set of infusions listed below.

Reconstitution of Part Doses: Because the dry powder in the vial displaces a set volume once it is in solution, this must be allowed for by calculating the volume of diluent to be added to ensure the correct dose is given.

250mg of stated activity displaces 0.2mL of diluent.

500mg of stated activity displaces 0.4mL of diluent.

1000mg of stated activity displaces 0.8mL of diluent.

e.g. Add 4.8mL of diluent to a 250mg vial to produce:

250mg in 5mL, 200mg in 4mL, 150mg in 3mL, 100mg in 2mL, 50mg in 1mL.

Add 4.6mL of diluent to a 500mg vial to produce 500mg in 5mL.

When the whole vial dose is to be given either add 5mL and withdraw and administer the entire contents or calculate the displacement and add a lesser volume of 5mL.

Solutions should be thoroughly mixed by vigorous shaking and checked for absence of particulate matter before use.

Contraindications

The use of this medicine is contraindicated in individuals with a history of hypersensitivity to beta-lactam antibiotics (e.g. penicillins and cephalosporins).

Warnings and Precautions

Dosage should be adjusted in patients with renal impairment (see dosage and administration).

In patients with reduced urine output crystalluria has been observed very rarely, predominantly with parental therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria.

Prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently.

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy.

Before commencing therapy with any penicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, cephamycins or penicillamine. Caution should also be taken in patients with a history of allergy, such as eczema, asthma, hay fever and hives. If any allergic reaction occurs, appropriate therapy should be instituted and **IBIAMOX** therapy discontinued.

Serious anaphylactoid reactions require emergency treatment with adrenalin, oxygen and intravenous steroids. Airway management including intubation should also be administered as indicated.

Use in Pregnancy and Lactation: Safety for use in pregnancy has not been established, although amoxicillin is known to diffuse across the placenta. The potential benefit should, therefore, be weighed against the potential risk before use. Very little amoxicillin appears in breast milk. Caution is, however, required as there may be a possibility of sensitisation, diarrhoea, candidiasis and skin rash in the infant.

As with any potent medicine, periodic assessment of renal, hepatic and haematopoietic function should be made during prolonged therapy. The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur (usually involving *Aerobacter*, *Pseudomonas* or *Candida*), the medicine should be discontinued and/or appropriate therapy instituted.

IBIAMOX should be given with caution to patients with infectious mononucleosis or lymphatic leukemia since they are especially susceptible to ampicillin induced skin rashes.

Adverse Effects

As with other penicillins, it may be expected that untoward reactions will be essentially limited to sensitivity phenomena.

They are more likely to occur in individuals who have previously demonstrated hypersensitivity to penicillins. The following adverse reactions have been reported as associated with the use of amoxicillin.

Blood and Lymphatic System Disorders:

Very rare: Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia.

Prolongation of bleeding time and prothrombin time

Immune system disorders

Very rare: As with other antibiotics, severe allergic reactions, including angioneurotic oedema, anaphylaxis, serum sickness and hypersensitivity vasculitis.

If a hypersensitivity reaction is reported, the treatment must be discontinued.

Nervous system disorders

Very rare: Hyperkinesia, dizziness and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Infections and Infestations

Very rare: Mucocutaneous candidiasis

Gastrointestinal disorders

Common: Diarrhoea and nausea.

Uncommon: Vomiting.

Very rare: Antibiotic associated colitis (including pseudomembranous colitis and haemorrhagic colitis). Black hairy tongue. Superficial tooth discolouration has been reported in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing

Hepato-biliary disorders

Very rare: Hepatitis and cholestatic jaundice. A moderate rise in AST and/or ALT. The significance of a rise in AST and/or ALT is unclear.

Skin and subcutaneous tissue disorders

Common: Skin rash.

Uncommon: Urticaria and pruritus.

Very rare: Skin reactions such as erythema multiforme, Stevens- Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis and acute generalised exanthematous pustulosis (AGEP).

Renal and Urinary tract disorders

Very rare: Interstitial nephritis, crystalluria

The incidence of these AEs was derived from clinical studies involving a total of approximately 6,000 adult and paediatric patients taking amoxicillin.

Interactions

BIAMOX should not be mixed with blood products or proteinaceous fluids such as protein hydrolysates, nor with intravenous lipid emulsions.

AMOXYCILLIN with:

Probenecid: Probenecid decreases renal tubular secretion of penicillins when used concurrently, resulting in increased and more prolonged amoxicillin serum concentrations and prolonged elimination half-life.

Chloramphenicol, Erythromycin, Sulfonamides or Tetracyclines: Since bacteriostatic agents may interfere with the bactericidal effect of penicillins in the treatment of meningitis or other situations where a rapid bactericidal effect is necessary, it is best to avoid concurrent therapy.

Estrogen Containing Oral Contraceptives: Concurrent administration with amoxicillin may decrease the effectiveness of oral contraceptives. Patients should be advised to use an alternative or additional method of contraception.

Allopurinol: There has been a report of an increased incidence of skin rash on concurrent administration.

Diagnostic Interference: **BIAMOX** interferes with positive direct antiglobulin (Comb's) test. It may also interfere with urine glucose determinations, due to high concentrations of amoxicillin in the urine.

It has also been found that serum alanine aminotransferase (ALT[SGOT]) and serum aspartate aminotransferase (AST[SGOT]) concentrations may be increased, following amoxicillin administration.

Total conjugated estriol, estriol-glucuronide, conjugated estrone and estradiol concentrations may be transiently decreased following **IBIAMOX** administration to pregnant women.

Overdosage

No incidence of overdosage has been reported.

Pharmaceutical Precautions

Store in a cool place, protected from moisture and light. Use prepared injections within 1 hour.

Medicine Classification

Prescription Medicine.

Package Quantities

IBIAMOX 250mg, 500mg and 1g injections are available in quantities of 10.

Further Information

Amoxicillin is (6R)-6-[alpha-D-(4-Hydroxy-phenyl)glycylamino]penicillanic acid, the formula of which is $C_{16}H_{19}N_3O_5S$. The molecular weight is 365.4.

1.06g of amoxicillin sodium is equivalent to approximately 1g of amoxicillin.

Infusion Fluids Compatible with Amoxicillin Sodium: When prepared for infusions, **IBIAMOX** should be administered within 1 hour, even though **IBIAMOX** maintains a satisfactory degree of activity at room temperature in various infusion fluids as follows:

Intravenous Fluids

Stability Time

Sodium chloride inj. (normal saline)	6 hours
Compound sodium chloride inj. (Ringer's solution)	6 hours
Sodium lactate inj.	3 hours
Compound sodium lactate inj. (Hartmann's solution)	3 hours
Dextrose inj. (5%)	1 hour
Sodium chloride and (4%) dextrose inj.	1 hour

Since **IBIAMOX** injection is relatively less stable in carbohydrate solutions, it is preferable to avoid using them. It may, however, be injected into the drip tubing of such an infusion or incorporated into a small volume of the solution and infused over a period of 30 to 60 minutes.

IBIAMOX injection is compatible with commonly used intravenous solutions.

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