

1. TRADE NAME OF THE MEDICINAL PRODUCT

Oramox 500 mg Hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains Amoxicillin Trihydrate equivalent to 500mg of anhydrous Amoxicillin.

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Capsules, hard (capsules)

Size 0 hard gelatin capsules with deep yellow opaque caps and ivory opaque bodies, marked 'Oramox 500' containing an off-white granular powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indication

Indications for use:

In the treatment of infections due to organisms sensitive to amoxicillin and in the oral prophylaxis of endocarditis related to dental procedures, and acute uncomplicated gonorrhoea.

4.2 Posology and method of administration

Adults and children over 10 years of age:

The usual total daily dosage is 750mg in three divided doses. In the treatment of uncomplicated gonorrhoea a single dose of 3g may be used.

Dosage may be doubled in cases of severe infections.

Children up to 10 years of age:

The usual total daily dosage is 375mg in divided doses (i.e. 125mg three times daily by the oral route). Children under 10 years half the adult dose and under 5 years Quarter adult dose.

In severe or recurrent acute otitis media, especially where compliance may be a problem, 750mg twice a day for two days may be used as an alternative course of treatment in children aged three to ten years.

Prophylaxis dose for Adults:

A single dose of 3g prior to dental procedure.

In patients with renal insufficiency:

Total daily dosage may need reduction if excretion of drug is delayed.

Renal impairment:

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

Glomerular filtration rate	Oral treatment
> 30 ml / min	No adjustment necessary
10-30 ml/min	Oramox. Max 500mg b.d.
< 10ml / min	Oramox: Max 500mg/day

Children under 40kg

Glomerular filtration rate	Oral treatment
> 30 ml / min	No adjustment necessary
10-30 ml/min	15 mg/kg given b.i.d. (maximum 500mg/twice daily)
< 10ml / min	15 mg/kg given as a single daily dose (maximum 500mg)

Amoxicillin Paediatric Suspension is recommended for children under 6 months of age.

In patients receiving peritoneal dialysis

Oral treatment: amox. Max. 500mg/day

Amoxicillin may be removed from the circulation by haemodialysis.

Simple acute urinary tract infection: two 3g doses with 10 – 12 hours between the doses.

Dental Abscess: two 3g doses with 8 hours between the doses.

Prophylaxis of endocarditis:

For dental procedures where an oral dose is appropriate:

Adults: 3g Oramox orally, 1 hour before procedure. A second dose may be given 6 hours later, if considered necessary.

Children: Aged 5-10: half the adult dose

Under 5: Quarter adult dose.

For oral administration only.

4.3 Contra-indications

Use in patients with hypersensitivity to any of the excipients.

Use in patients with hypersensitivity to beta-lactam antibiotics including penicillins, ampicillin or to cephalosporins.

4.4 Special warnings and precautions for use

Prolonged use of an anti-infective may occasionally result in overgrowth of non-susceptible organisms and those resistant to anti-infective.

Dosage should be adjusted in patients with renal impairment (see Section 4.2).

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

In patients with renal impairment, the rate of excretion of amoxicillin will be reduced depending on the degree of impairment and it may be necessary to reduce the total daily unit amoxicillin dosage accordingly.

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins. These reactions are more likely to occur in persons with a history of penicillin hypersensitivity and/ or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of severe reactions when treated with cephalosporin. Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens.

If allergic reaction occurs, amoxicillin should be discontinued and appropriate therapy should be instituted and discontinuance of amoxicillin therapy considered.

Serious anaphylactoid reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should be administered as indicated.

In patients with reduced urine output crystalluria has been observed very rarely predominantly with parenteral 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.

Amoxicillin should be avoided if infectious mononucleosis (glandular fever) is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of amoxicillin.

4.5 Interactions with other medicaments and other forms of interaction

When administered concurrently, the following drugs may interact with amoxicillin:

Oral Contraceptives:

In common with other broad spectrum antibiotics amoxicillin may affect the gut flora, leading to lower oestrogen reabsorption and reduce the efficacy of oral contraceptives and patients should be warned accordingly.

Bacteriostatic antibiotics:

Chloramphenicol, erythromycins, sulfonamides or tetracyclines may interfere with the bactericidal effects of penicillins. This has been demonstrated in vitro; however, the clinical significance of this interaction is not well documented.

Probenecid:

Probenecid may decrease renal tubular secretion of amoxicillin resulting in increased blood levels and/or amoxicillin toxicity.

Drug/Laboratory Test Interactions:

After treatment with amoxicillin, a false-positive reaction for glucose in the urine may occur with copper sulphate tests (Benedict's solution, Fehling's solution, or Clinitest tablets) but not with enzyme based tests such as Clinistix and Tes-Tape.

Concurrent administration of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Concurrent use of penicillins (including amoxicillin) with methotrexate, can reduce the clearance of methotrexate from the body.

4.6 Pregnancy and lactation

Use in pregnancy:

Animal studies with Amoxicillin have shown no teratogenic effects. The product has been in extensive clinical use since 1972 and its suitability in human pregnancy has been well documented in clinical studies. Amoxicillin may be used in pregnancy when the potential benefits outweigh the potential risks associated with treatment.

Use in lactation:

Amoxicillin is excreted in breast milk, presenting the risk of candidiasis and of central nervous system toxicity due to prematurity of the blood-brain barrier. Amoxicillin may be administered during the period of lactation. With the exception of the risk of sensitisation associated with the excretion of trace quantities of amoxicillin in breast milk, there are no known detrimental effects for the infant.

4.7 Effects on ability to drive and use machines

Adverse effects on the ability to drive or operate machinery have not been observed.

4.8 Undesirable effects

The following convention has been utilised for the classification of undesirable effects:

Very common (more than 1/10), common (more than 1/100, less than 1/10), uncommon (more than 1/1000, less than 1/100), rare (more than 1/10,000, less than 1/1000), very rare (less than 1/10,000).

The majority of the side-effects listed below are not unique to amoxicillin and may occur when using other penicillins.

Unless otherwise stated, the frequency of adverse events (AEs) has been derived from more than 30 years of post-marketing reports.

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 (see Warnings and Precautions), serum sickness and hypersensitivity vasculitis.

If a hypersensitivity reaction is reported, the treatment must be discontinued. (See also Skin and subcutaneous tissue disorders).

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 pseudomembraneous 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 (for suspension and chewable tablet formulations only)

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).

(See also Immune system disorders).

Renal and Urinary tract disorders

Very rare: Interstitial nephritis, crystalluria (see Overdosage)

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

4.9 Overdose

Gross overdosage will produce very high urinary concentrations, more so after parenteral administration. Symptoms of water/electrolyte imbalance should be treated symptomatically. Problems are unlikely to occur if adequate fluid intake and urinary output are maintained; however amoxicillin crystalluria in some cases leading to renal failure, has been observed (see Section 4.4, Special Warnings and Special Precautions for Use). More specific measures may be required in patients with impaired renal function: the antibiotic is removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Amoxicillin is a broad-spectrum antibiotic which possesses the safety profile of the penicillins and is rapidly bactericidal against a wide range of Gram-negative and Gram-positive organisms.

Amoxicillin is semisynthetic penicillin, which is acid resistant and has a similar antibacterial spectrum to Ampicillin.

It is, however, better absorbed after oral administration, yielding blood levels approximately twice as high as those obtained with similar doses of Ampicillin.

Amoxicillin is used for the same purposes as Ampicillin and is especially suitable for the treatment of infections of the urinary and respiratory tracts by Ampicillin sensitive organisms.

5.2 Pharmacokinetic properties

Absorption:

Amoxicillin is stable to gastric acid and 50 - 90% of a dose is absorbed after oral administration: absorption is more complete than that of Ampicillin and it is not greatly influenced by the presence of food. Amoxicillin is well absorbed by the oral and parenteral routes, peak blood levels are achieved one to two hours after administration. Oral administration produces high serum levels independent of the time at which the food is taken.

Blood Concentration:

After an oral dose of 500mg, peak serum concentration of 3 to 20ug/ml are attained in 1 to 2 hour, detectable concentrations are present after 8 hours. Peak concentrations occur earlier in children and infants, but later in neonates.

Amoxicillin gives good penetration into the bronchial secretions and the high urinary concentrations of unchanged antibiotic.

Half-life:

Serum half-life, 1 hour which may be increased to 15 hours in renal failure.

Distribution:

Enters most tissues and fluid but is not detectable in the cerebrospinal fluid even when meninges are inflamed; crosses the placenta and small amounts are secreted in the milk; volume of distribution at steady-state serum concentrations, about 0.3 litres/kilogram body weight; protein binding, 15 - 25% bound to plasma protein.

Metabolic Reactions:

Metabolised to inactive metabolites and 10 - 25% appears to be converted to penicilloic acid.

Excretion:

35 - 45% is excreted in the urine after an oral dose; urinary excretion is delayed by probenecid and it also occurs more slowly in the newborn; small amounts are excreted in the bile.

5.3 Preclinical safety data

No further information other than that which is included in the Summary of Product Characteristics No further information other than that which is included in the Summary of Product Characteristics

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium Stearate
Maize Starch

Capsule body
Red Iron Oxide E172
Yellow Iron Oxide E172

Titanium Dioxide E171
Gelatin

Capsule Cap
Yellow Iron Oxide E172
Titanium Dioxide E171
Gelatin

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package to protect from light and moisture. Keep the container tightly closed.

6.5 Nature and contents of container

Polypropylene securitainers with tamper evident polypropylene caps.
Pack sizes: 50, 100 and 500 capsules. Not all pack sizes may be marketed

6.6 6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7. MARKETING AUTHORIZATION HOLDER

Antigen Pharmaceuticals Ltd.,
Roscrea,
Co.Tipperary.

8. MARKETING AUTHORIZATION NUMBER

PA 73/113/2

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

Date of first authorisation: 27th September 1988
Date of last Renewal: 27th September 1988

10. DATE OF (PARTIAL) REVISION OF THE TEXT

May 2010