SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Oramox 250mg Hard Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains Amoxicillin Trihydrate equivalent to 250mg of anhydrous Amoxicillin.

For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Capsules, hard

Size 2 hard gelatin capsules with scarlet caps and ivory bodies, printed in black with 'Amox 250' and containing an off-white granular powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Oramox is a broad spectrum antibiotic, indicated for the treatment of commonly occurring bacterial infections such as:
• Upper respiratory tract infections
• Otitis media
• Acute and chronic bronchitis
• Lobar and bronchopneumonia
• Cystitis, urethritis, pyelonephritis
• Bacteriuria in pregnancy
• Gynaecological infections including puerperal sepsis and septic abortion
• Gonorrhoea
• Peritonitis
• Intra-abdominal sepsis
• Septicaemia
• Bacterial endocarditis (see also Oral prophylaxis of endocarditis)
• Typhoid and paratyphoid fever
• Skin and soft tissue infections
• Dental abscess (as adjunct to surgical management)
In children with urinary tract infection, the need for investigation should be considered.
Parenteral therapy is indicated if the oral route is considered impracticable or unsuitable and particularly for the urgent treatment of severe episodes of the above conditions.
Oral prophylaxis of endocarditis: Oramox may be used for the prevention of bacteraemia associated with the procedures such as dental extraction, in patients at risk of developing bacterial endocarditis.

4.2 Posology and method of administration

Oramox Capsules are for oral use.

The absorption of Oramox is virtually unimpaired by the presence of food.
Adults and children weighing over 40kg:
Standard adult dosage:
The usual daily dosage is 750mg in divided doses (i.e. 250mg three times daily by the oral route).
In cases of severe infection the dosage may be doubled, or amoxicillin given by injection.

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High dosage therapy (maximum recommended oral dosage of 6g daily in divided doses): A dosage of 3g twice daily is recommended in appropriate cases for the treatment of severe or recurrent purulent infection of the respiratory tract.

Short course therapy:
Simple acute urinary tract infection: two 3g doses with 10-12 hours between the doses.
Gonorrhoea: 3g as a single dose.
Dental Abscess: two 3g doses with 8 hours between the doses.
Prophylaxis of endocarditis
For dental procedures where an oral dose is appropriate:
Adults including children weighing over 40kg:
3g dose followed by (6 hours later) a further 3g dose (or a 1g IM if oral dose not tolerated) if necessary.

Paediatric population
Children weighing < 40 kg
The daily dosage for children is 40 - 90 mg/kg/day in two to three divided doses* (not exceeding 3 g/day) depending on the indication, severity of the disease and the susceptibility of the pathogen (see special dosage recommendations below and sections 4.4, 5.1 and 5.2).
*PK/PD data indicate that dosing three times daily is associated with enhanced efficacy, thus twice daily dosing is only recommended when the dose is in the upper range.
Children weighing more than 40 kg should be given the usual adult dosage.

Special dosage recommendation
Tonsillitis: 50 mg/kg/day in two divided doses.
Acute otitis media: In areas with high prevalence of pneumococci with reduced susceptibility to penicillins, dosage regimens should be guided by national/local recommendations.
Early Lyme disease (isolated erythema migrans): 50 mg/kg/day in three divided doses, over 14-21 days.

Prophylaxis for endocarditis:
Paediatric population

50 mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure

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Dosage in impaired renal function:

The dose should be reduced in patients with severe renal function impairment. In patients with creatinine clearance of less than 30ml/min an increase in the dosage interval and a reduction in the total daily dose is recommended (see section 4.4 and 5.2)

Renal impairment in adults:

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

Renal impairment in children under 40kg:

Creatinine clearance ml/min	Dose	Interval between administration
> 30	Usual dose	No adjustment necessary
10-30	Usual dose	12h (corresponding to 2/3 of the dose)
< 10	Usual dose	24h (corresponding to 1/3 of the dose)

For small children (younger than 6 years of age) appropriate paediatric formulation should be used.

4.3 Contra-indications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1. Use in patients with a history of hypersensitivity to beta-lactam antibiotics including penicillins, ampicillin or cephalosporins.

4.4 Special warnings and precautions for use

Before initiating therapy with amoxicillin, careful enquiry should be made concerning previous hypersensitivity
reactions to penicillins, cephalosporins. Cross-sensitivity between penicillins and cephalosporins is well documented.

Serious and occasionally fatal hypersensitivity (anaphylaxis) 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 with multiple allergens. Attention should also be paid to possible cross-reactivity with other beta-lactam antibiotics e.g. cephalosporins (see section 4.3)

If an allergic reaction occurs, amoxicillin should be discontinued and appropriate therapy should be instituted.

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.

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

Abnormal prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving amoxicillin and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently.
Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

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

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.

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

Precaution should be taken in premature children and during the neonatal period: renal, hepatic and haematological functions should be monitored.

4.5 Interaction with other medicinal products 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.

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

Methotrexate
Interaction between amoxicillin and methotrexate leading to methotrexate toxicity has been reported. Serum methotrexate levels should be closely monitored in patients who receive amoxicillin and methotrexate simultaneously. Amoxicillin decreases the renal clearance of methotrexate, probably by competition at the common tubular secretion system.

Anticoagulants
In the literature there are rare cases of increased international normalised ratio in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin.

4.6 Fertility, pregnancy and lactation

Pregnancy
The product should not be used during pregnancy unless considered essential by the physician. 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.

Breast-feeding
Amoxicillin may be administered during the period of lactation. With the exception of the risk of sensitisation and of
central nervous system toxicity (due to prematurity of the blood-brain barrier) 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

Amoxicillin has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

Evaluation of undesirable effects is based on the following frequency information: very common (> 1/10); common(1/100 to <1/10); uncommon (1/1,000 to <1/100); rare (1/10,000 to <1/1,000); very rare (<1/10,000); not known (frequency cannot be estimated from available data).

The majority of 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. (see section 4.4 Special warnings and precautions for use).

Immune System disorders:
Very rare: As with other antibiotics, severe allergic reactions including angioneurotic oedema, anaphylaxis (see Warnings and Precaution), 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. Aseptic meningitis.

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 (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 Overdose).

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

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Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued
monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any
suspected adverse reactions via:
HPRA Pharmacovigilance
Earlsfort Terrace
IRL – Dublin 2
Tel: +353 1 6764971
Fax +353 1 6762517

Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

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 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.

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.

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 probenecide and it also occurs more slowly in the newborn; small amounts are excreted in the bile.

In preterm infants with gestational age 26-33 weeks, the body clearance after intravenous dosing of amoxicillin, day 3 of life, ranged between 0.75-2ml/min, very similar to the inulin clearance (GFR) in this population. Following oral administration, the absorption pattern and the bioavailability of amoxicillin in small children may be different to that of adults. Consequently, due to the decreased CL, the exposure is expected to be elevated in this group of patients, although this increase in exposure may in part be diminished by decreased bioavailability when given orally.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium Stearate
Maize Starch

Capsule Shell
Erythrosine E127
Quinoline Yellow E104
Titanium Dioxide E171
Red Iron Oxide E172
Gelatin

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

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

6.5 Nature and contents of container

An opaque white polypropylene securitainer with a polyethylene air proof security cap.
Pack sizes 100, 500 and 1,000capsules.jayfilla.

Not all pack sizes may be marketed.

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 AUTHORISATION HOLDER

Athlone Laboratories Limited,
Ballymurray,
Co. Roscommon,

8 MARKETING AUTHORISATION NUMBER

PA 298/19/3

9 DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of first authorisation: 27th September 1988
Date of last renewal: 27th September 2003

10 DATE OF REVISION OF THE TEXT

March 2015