DATA SHEET

m-Amoxicillin

QUALITATIVE AND QUANTITATIVE COMPOSITION
Each Filled capsule contains Amoxicillin Trihydrate BP/EP equivalent to Amoxicillin 250 mg and Amoxicillin 500 mg
For a full list of excipients, see Pharmaceutical Particulars.

PHARMACEUTICAL FORM
Capsules:
Amoxicillin 250 mg Capsule: Red / Buff coloured size ‘2’ capsules containing white to off white powder printed with ‘AMOXY 250’ in black ink.
Amoxicillin 500 mg Capsules: Red / Buff Coloured size ‘0’ Capsules containing white to off white powder printed with ‘AMOXY 500’ in black ink.

CLINICAL PARTICULARS
Therapeutic indications
Amoxicillin is indicated for the treatment of the following infections due to susceptible strains of sensitive organisms:
Upper Respiratory Infections: Otitis media, pharyngitis, sinusitis and tonsillitis.
Lower Respiratory Infections: Bronchitis, bronchopneumonia and lobar pneumonia.
Urinary Tract Infections: Cystitis, cysto-pyelitis, urethritis, and gonococcal urethritis.
Prophylaxis: against α-haemolytic (viridans group) and β-haemolytic Streptococci before dental, oral or upper respiratory tract surgery or instrumentation.
Prophylaxis: of bacterial endocarditis in patients with any of the following conditions: congenital cardiac malformations, rheumatic and other acquired valvular lesions, prosthetic heart valves, previous history of bacterial endocarditis, hypertrophic cardiomyopathy, surgically constructed systemic-pulmonary shunts, mitral valve prolapse with valvular regurgitation or mitral valve prolapse without valvular regurgitation but associated with thickening and/or redundancy of the valve leaflets.
Amoxicillin is further indicated for the treatment of cutaneous infections. In emergency cases where the causative organism is not yet identified, therapy may be initiated with amoxicillin on the basis of clinical judgement, while awaiting the results of bacteriologic studies to determine its antimicrobial sensitivity.

Dosage and method of administration
Dosage
Amoxicillin can be administered orally independent of meals. Therapy should be maintained for a minimum of 5 days. Treatment should be continued for a minimum of 96 hours beyond the time the patient becomes asymptomatic or after evidence of bacterial eradication is observed. At least 10 days treatment is recommended for any infection caused by beta-haemolytic streptococci to prevent the occurrence of acute rheumatic fever or glomerulonephritis.
Infections of the upper respiratory or genitourinary tracts, skin and soft tissues, due to susceptible strains of the causative organism:
Adults: 250 mg every 8 hours.
Children < 20 kg: 25 mg/kg/day in divided doses every 8 hours.
In severe infections or infections associated with organisms where sensitivity determinations require higher blood concentrations:
Adults: 500 mg every 8 hours.
Children < 20 kg: 50 mg/kg/day in divided doses every 8 hours; this dosage should not exceed the recommended adult dosage.
Infections of the lower respiratory tract due to susceptible strains of the causative organism, and acute otitis media:
Adults: 500 mg every 8 hours.
Children <20 kg: 50 mg/kg/day in divided doses every 8 hours; this dosage should not exceed the recommended adult dosage.
High Dosage Therapy: An adult dosage of 3g twice daily is recommended in appropriate cases for the treatment of severe or recurrent purulent infection of the respiratory tract.

Urethritis due to non-penicillinase producing N. gonorrhoea acquired in areas with active monitoring for resistance to penicillin and where the percentage of penicillin-resistant isolates is <3.0%:
Adults and children >45 kg: 3 g as a single oral dose; 1 g of oral probenecid should be administered concomitantly as well as appropriate therapy for presumptive or proven infection with C. trachomatis.
Children <45 kg: a single 50 mg/kg dose (maximum 3 g) of amoxicillin given with a single 25 mg/kg (up to 1 g) dose of probenecid. However, probenecid is not recommended in children under 2 years of age. Appropriate therapy of presumptive or proven infection with C. trachomatis should be included as well.
Before prescribing amoxicillin, dark field examinations should be carried out in those cases where syphilis is also suspected and monthly serologic tests should be carried out for a minimum of 4 months.

Acute, uncomplicated lower urinary tract infections:
Adults: 3g as a single dose.
In the treatment of chronic urinary tract infections, frequent bacteriologic and clinical evaluations are necessary. Doses smaller than those recommended above should not be used. In stubborn infections, therapy may be required for several weeks, sometimes at doses higher than those recommended. Concurrent bacteriologic sensitivity monitoring is recommended. It may be necessary to continue clinical and/or bacteriologic follow-up for several months after cessation of therapy.

For prevention of endocarditis:
Patient not having a general anaesthetic:
Adults: 3 g orally one hour before the procedure. A second dose may be given 6 hours later if considered necessary.
Children: For children under 5 administer quarter the adult dose and for children aged 5 to 10 administer half the adult dose.

Patient having a general anaesthetic - oral antibiotics appropriate:
Adults: 3g orally 4 hours prior to anaesthesia followed by 3g orally 6 hours after the initial dose.
Children: For children under 5 administer quarter the adult dose and for children aged 5 to 10 administer half the adult dose.
Note: The children's dose is intended for individuals whose weight will not cause dosage to be calculated greater than that recommended for adults. Children weighing more than 20 kg should be dosed according to the adult recommendations.

Dosage in renal failure:
The relative dose interval for amoxicillin is 4 hours; thus, in patients with renal failure in whom the half life is 6 hours the dosage interval is 24 hours and it may be necessary to reduce the total daily dosage. In patients with a creatinine clearance of more than 30mL/min no dosage adjustment is required. For patients with a creatinine clearance between 10 and 30mL/min the maximum recommended dose is 500mg twice daily. For patients with a creatinine clearance of less than 10mL/min the maximum recommended dose is 500mg per day. In patients receiving peritoneal dialysis the maximum recommended daily dose is 500mg. Amoxicillin may be removed from the system by haemodialysis.

Contraindications
Amoxicillin is contraindicated in patients with:
Hypersensitivity to penicillin; a cross-allergy to other beta-lactams such as cephalosporins
should be taken into account. Viral infections, acute lymphatic leukaemia, or infectious mononucleosis (due to an increased risk of erythematous skin rashes)

**Special warnings and precautions for use**

Patients suffering from severe gastrointestinal disturbances with diarrhoea and vomiting should not be treated with oral amoxicillin, due to the risk of reduced absorption. In these cases a parenteral treatment with amoxicillin is advisable.

Amoxicillin should be used with caution in patients with an allergic diathesis and asthma. In patients with renal function impairment, the excretion of amoxicillin will be delayed and, depending on the degree of impairment, it may be necessary to reduce the total daily dosage (see Dosage and Method of Administration).

The prolonged use of amoxicillin may occasionally result in an overgrowth of nonsusceptible organisms or yeasts. Patients should therefore carefully be watched for superinfections. The occurrence of anaphylactic shock and other severe allergic reactions is rare following oral administration of amoxicillin. However, if such reactions occur, appropriate emergency treatment measures must be taken: i.v. administration of epinephrine, followed by antihistaminic drugs, volume substitution and administration of glucocorticoids. Patients should be kept under close observation, and further therapeutic measures (artificial respiration, oxygen) should be administered as required.

The presence of high urinary concentrations of amoxicillin can cause precipitation of the product in urinary catheters. Therefore, catheters should be visually inspected at intervals. At high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to minimize the possibility of amoxicillin crystalluria.

**Interaction with other medicinal products and other forms of interaction**

In common with other broad spectrum antibiotics, amoxicillin may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

Concurrent administration of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions. Prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently.

An increase in the absorption of digoxin may occur on concurrent administration with amoxicillin. The antibacterial action of amoxicillin may be antagonised on co-administration with macrolides, tetracyclines, sulphonamides or chloramphenicol.

It is recommended that when testing for the presence of glucose in urine during amoxicillin treatment, enzymatic glucose oxidase methods should be used. Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods.

Probenecid decreases the renal tubular secretion of amoxicillin. Concurrent use with amoxicillin may result in increased blood concentrations of amoxicillin and prolonged exposure.

**Pregnancy and lactation**

**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. When antibiotic therapy is required during pregnancy, Amoxicillin may be considered appropriate when the potential benefits outweigh the potential risks associated with treatment.

**Lactation**

Amoxicillin may be given during 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 breast-fed infant.
Effects on ability to drive and use machines
Adverse effects on the ability to drive or operate machinery have not been observed. Nevertheless, consideration should be given to the potential for amoxicillin to cause dizziness and convulsions (see Adverse Effects).

Adverse effects
The following convention has been utilised for the classification of adverse effects:-
Very common (>1/10), common (>1/100, <1/10), uncommon (>1/1000, <1/100), rare (>1/10,000, <1/1000), very rare (<1/10,000)
Most side effects listed below are not unique to amoxicillin and may occur when using other pencillins.
Unless otherwise stated, the frequency of adverse events 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.

Immune system disorders
Very rare: As with other antibiotics, severe allergic reactions, including angioneurotic oedema, anaphylaxis (see Special Warnings and Precautions for Use), 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.

Gastrointestinal disorders
Common: Diarrhoea and nausea.
Uncommon: Vomiting.
Very rare: Mucocutaneous candidiasis and antibiotic associated colitis (including pseudomembraneous colitis and haemorrhagic colitis).

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.

Other undesirable effects
Prolonged and repeated use of the preparation can result in superinfections and colonization with resistant organisms or yeasts such as oral and vaginal candidiasis.

Overdose
Gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident and should be treated symptomatically with attention to the water/electrolyte balance. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed (see Special
Amoxicillin may be removed from the circulation by haemodialysis.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Pharmacotherapeutic group: Penicillins with extended spectrum
ATC Code J01CA04
Mode of action
Amoxicillin is an aminopenicillin that exerts its bactericidal action by inhibition of the synthesis of the bacterial cell wall.
PK/PD relationship
Clinical efficacy of beta-lactams appears to be related to time that drug concentrations in the blood exceed the MIC for a specific micro-organism.
Mechanisms of resistance
Bacteria may be resistant to amoxicillin owing to:
- production of beta-lactamases that hydrolyse aminopenicillins
- alterations in penicillin-binding proteins
- impermeability of the bacteria to the drug
- drug efflux pumps.
One or more of these mechanisms may co-exist in the same organism leading to variable and unpredictable cross-resistance to other beta-lactams and to antibacterial drugs of other classes.
Breakpoints
The MIC breakpoints for susceptible organisms vary according to species. S (sensitive) and R (resistant).
Entrobacteriaceae are considered susceptible when inhibited at ≤ 8 mg/L amoxicillin.
From CLSI recommendations and using CLSI-specified methods:
- *M. catarrhalis* (β-lactamase negative) S ≤ 0.25mg/L; R ≥ 0.5mg/L;
- *H. influenzae* (β-lactamase negative) S ≤1mg/L; R ≥ 4mg/L;
- *S. pneumoniae* S≤ 0.5mg/L; R ≥ 2mg/L.

Susceptibility:
The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.
Commonly susceptible species
- Gram-positive aerobes
  - *Enterococcus faecalis*
  - *Streptococcus agalactiae*
  - *Streptococcus pyogenes*
- Gram-negative aerobes
  - *Neisseria meningitidis*
  - Anaerobes
  - *Clostridium perfringens*
  - Peptostreptococci

In some instances and in some regions almost all strains of certain species are now resistant to aminopenicillins. Therefore it is recommended that amoxicillin should not be used to treat any of the following *Species for which acquired resistance may be a problem* unless laboratory test results have confirmed susceptibility:
*Species for which acquired resistance may be a problem*

**Aerobes**
- *Staphylococcus aureus*
- *Streptococcus pneumoniae*
- *Streptococcus viridans*
- *Escherichia coli*
- *Haemophilus influenzae*
- *Haemophilus parainfluenzae*
- *Klebsiella spp*
- *Moraxella catarrhalis*
- *Neisseria gonorrhoeae*
- *Proteus mirabilis*
- *Proteus spp* (indole positive)
- *Proteus vulgaris*
- *Providencia spp*
- *Anaerobes*
- *Bacteroides spp.*
- *Fusobacterium spp*

**Inherently resistant organisms**

- Gram-negative aerobes
  - *Acinetobacter spp*
  - *Citrobacter spp*
  - *Enterobacter spp*
  - *Providencia spp*
- *Pseudomonas spp*
- *Serratia spp*
- *Others*
- *Chlamydia*
- *Mycoplasma*
- *Rickettsia*

**Pharmacokinetic properties**

**Absorption:**
The absolute bioavailability of amoxicillin varies between 75 and 90%. Bioavailability (as assessed by pharmacokinetic parameters AUC and/or recovery in urine) is linearly proportional to the dose of amoxicillin between 250 mg and 750 mg. The extent of absorption of amoxicillin decreases at higher doses. Absorption of amoxicillin is not affected by concomitant food intake. Oral administration of a single dose of 500 mg amoxicillin results in plasma concentrations of 6 - 11 mg/l. After administration of a single dose of 3 g amoxicillin, the plasma concentrations reach 27 mg/l. Peak plasma concentrations are present about 1-2 hours after administration.

**Distribution:**
Protein binding for amoxicillin is approximately 17%. Therapeutic drug levels are rapidly achieved in serum, lung tissue, bronchial secretions, middle ear fluid, bile and urine. Amoxicillin can penetrate inflamed meninges and enter the cerebrospinal fluid. Amoxicillin crosses the placenta and a small percentage is excreted into the breast milk.

**Biotransformation and elimination:**
Amoxicillin is mainly excreted via the kidney. About 60-80% of an oral dose of amoxicillin is excreted in the urine in unchanged form within 6 hours of administration. A small percentage is excreted in the bile. About 7 - 25% of the administered dose is metabolised to inactive penicilloic acid. The serum half-life in patients with normal renal function is about 1 – 1.5 hour. The serum half-life of amoxicillin in patients with end-stage renal failure is between 5 to 20 hours. Amoxicillin may be removed from the circulation by haemodialysis.
Preclinical safety data
Not Applicable

PHARMACEUTICAL PARTICULARS

List of excipients
Each 250mg and 500mg capsule contains:
Croscarmellose Sodium, Magnesium stearate.
Capsule shell components:
Cap:
Brilliant blue E133
Carmoisine E122
Sunset yellow E110
Titanium dioxide E171
Body:
Quinoline yellow E104
Sunset yellow E110
Titanium dioxide E171
Shell composition:
Purified Water
Methyl Parahydroxybenzoate E218
Propyl Parahydroxybenzoate E216
Gelatin (TSE Free)
Sodium lauryl sulphate
Printing ink components:
Absolute alcohol
Isopropyl alcohol
Shellac
Black iron oxide
Butyl alcohol
Propylene glycol

Incompatibilities
Not applicable

Shelf life
HDPE bottle: 24 months

Special precautions for storage
Store below 30°C

Nature and contents of container
Pack sizes of 500 capsules are available in HDPE screw-top containers with an aluminium tagger

Special precautions for disposal
No special requirements.

Further Information
This product may not be interchangeable with similar products on the New Zealand market.

Medicine Classification
Prescription Medicine

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**DATE OF PREPARATION**  
14 July 2010