SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Amoxicillin 500 mg Capsules BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Amoxicillin 500mg Capsules contain 500mg amoxicillin per capsule
Amoxicillin is present as trihydrate)
For full list of excipients see section 6.1

3 PHARMACEUTICAL FORM

Capsule.
Red/buff size 0 hard gelatin capsule containing a white to off white powder.
Printed with “AMOXY 500”.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment for infection: Amoxicillin 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
Chronic bronchial sepsis
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
Typhoid and paratyphoid fever
Skin and soft tissue infections
Dental abscess (as an adjunct to surgical management)
Helicobacter pylori eradication in peptic (duodenal and gastric) ulcer disease.

In children with urinary tract infection the need for investigation should be considered.

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

Consideration should be given to official local guidance (e.g. national requirements) on the appropriate use of antibacterial agents. Susceptibility of the causative organism to the treatment should be tested (if possible), although the therapy may be initiated before the results are available.

4.2 Posology and method of administration

Treatment of infection:

Adult dosage *(including elderly patients):*

Standard adult dosage: 250 mg three times daily, increasing to 500 mg three times daily for more severe infections.

High dose therapy (maximum recommended oral dosage 6 g 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 doses. Dental abscess: two 3 g doses with 8 hours between the doses.
Gonorrhoea: Single 3g dose.

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

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

Helicobacter eradication in peptic (duodenal and gastric) ulcer disease:

Amoxicillin is recommended at a dose of twice daily in association with a proton pump inhibitor and antimicrobial agents as detailed below:

Omeprazole 40 mg daily, Amoxicillin 1g BID, Clarithromycin 500mg BID x 7days

Or

Omeprazole 40 mg daily, Amoxicillin 750mg – 1g BID, Metronidazole 400mg TID x 7days

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 dose.

Renal impairment in children under 40kg:

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

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

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. 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 3 to 10 years.

Early Lyme disease (isolated erythema migrans): 50 mg/kg/day in three divided doses, over 14-21 days.
Prophylaxis for endocarditis: 50 mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure.

Prophylaxis of endocarditis:

CONDITION		ADULTS' DOSAGE (INCLUDING ELDERLY)	CHILDREN'S DOSAGE (< 40kg)	NOTES
Dental procedures: prophylaxis for patients undergoing extraction, scaling or surgery involving gingival tissues and who have not received a penicillin in the previous month. (N.B. Patients with prosthetic heart valves should be referred to hospital - see below).	Patient not having general anaesthetic.	3 g 'Amoxicillin' orally, 1 hour before procedure. A second dose may be given 6 hours later, if considered necessary.	50mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure	Note 1. If prophylaxis with 'Amoxicillin' is given twice within one month, emergence of resistant streptococci is unlikely to be a problem. Alternative antibiotics are recommended if more frequent prophylaxis is required, or if the patient has received a course of treatment with a penicillin during the previous month. Note 2 To minimise pain on injection, 'Amoxicillin' may be given as two injections of 500 mg dissolved in sterile 1% lignocaine solution (see *Administration*).
	Patient having general anaesthetic: if oral antibiotics considered to be appropriate.	Initially 3 g 'Amoxicillin' orally 4 hours prior to anaesthesia, followed by 3 g orally (or 1 g IV or IM if oral dose not tolerated) as soon as possible after the operation.		
	Patient having general anaesthetic: if oral antibiotics not appropriate.	1 g 'Amoxicillin' IV or IM immediately before induction; with 500 mg orally, 6 hours later.		
Dental procedures : patients for whom referral to hospital is recommended: a) Patients to be given a general anaesthetic who have been given a penicillin in the previous month. b) Patients to be given a general anaesthetic who have a prosthetic		Initially: 1 g 'Amoxicillin' IV or IM with 120 mg gentamicin IV or IM immediately prior to anaesthesia (if given) or 15 minutes prior to dental	50mg amoxicillin/kg body weight given as a single dose one hour preceeding the surgical procedure	See Note 2. Note 3. 'Amoxicillin' and gentamicin should not be mixed in the same syringe. Note 4. Please consult the appropriate data

heart valve. c) Patients who have had one or more attacks of endocarditis.		procedure. Followed by (6 hours later): 500 mg 'Amoxicillin' orally.		sheet for full prescribing information on gentamicin.
Genitourinary Surgery or Instrumentation: prophylaxis for patients who have no urinary tract infection and who are to have genito-urinary surgery or instrumentation under general anaesthesia. In the case of *Obstetric and Gynaecological Procedures* and *Gastrointestinal Procedures*– routine prophylaxis is recommended only for patients with prosthetic heart valves.		Initially: 1 g 'Amoxicillin' IV or IM with 120 mg gentamicin IV or IM, immediately before induction. Followed by (6 hours later): 500 mg 'Amoxicillin' orally or IV or IM according to clinical condition.		See Notes 2, 3 and 4 above.
Surgery or Instrumentation of the Upper Respiratory Tract	Patients other than those with prosthetic heart valves.	1 g 'Amoxicillin' IV or IM immediately before induction; 500 mg 'Amoxicillin' IV or IM 6 hours later.	50mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure	See Note 2 above. Note 5. The second dose of 'Amoxicillin' may be administered orally as 'Amoxicillin' Syrup SF or Amoxicillin oral suspension.
	Patients with prosthetic heart valves.	Initially: 1 g 'Amoxicillin' IV or IM with 120 mg gentamicin IV or IM, immediately before induction; followed by (6 hours later) 500 mg 'Amoxicillin' IV or IM.	50mg amoxicillin/kg body weight given as single dose one hour preceding the surgical procedure	See Notes 2, 3, 4 and 5 above.

Administration: Oral:
Treatment should be continued for 2 to 3 days following the disappearance of symptoms. It is recommended that at least 10 days treatment be given for any infection caused by beta-haemolytic streptococci in order to achieve eradication of the organism.

4.3 Contraindications

Amoxicillin is a penicillin and should not be given to penicillin-hypersensitive patients. Attention should be paid to possible cross-sensitivity with other beta-lactam antibiotics eg. 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.

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of hypersensitivity to beta-lactam antibiotics (see 4.3).

Erythematous (morbilliform) rashes have been associated with glandular fever in patients receiving amoxicillin.

Prolonged use may also occasionally result in overgrowth of non-susceptible organisms.

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 (see Section 4.9 Overdose).

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 (see section 4.2).

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 concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation (see sections 4.5 and 4.8).

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

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

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.

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 (see sections 4.4 and 4.8).

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.

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

Use in 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.

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 (>1/10), common (>1/100, <1/10), uncommon (>1/1000, <1/100), rare (>1/10,000, <1/1000), very rare (<1/10,000)

The majority of 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.

Infections and infestations

Very rare: Mucocutaneous candidiasis

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 Section 4.4 - Special Warnings and Precautions for Use), serum sickness and hypersensitivity vasculitis.

Flare of DRESS (Drug Rash with Eosinophilia and Systemic Symptoms) syndrome and development of amoxicillin hypersensitivity have been very rarely reported in patient with previous history of DRESS syndrome with other drugs.

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

Clinical Trial Data

*__Common:__ Diarrhoea and nausea.
__*Uncommon__: Vomiting.

Post-marketing Data

Very rare: Mucocutaneous candidiasis and 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.

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

Clinical Trial Data

***Common**: Skin rash
***Uncommon**: Urticaria and pruritus

Post-marketing Data

Very rare: Skin reactions such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis and acute generalised exanthematous pustulosis (AGEP). Amoxicillin has been reported to be rarely associated with DRESS syndrome in patients with predisposing factors (See also Immune system disorders).

Renal and urinary tract disorders

Very rare: Interstitial nephritis.
Very rare: Crystalluria (see Section 4.9 Overdose).

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

4.9 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 Section 4.4 Special warnings and special precautions for use).

Amoxicillin may be removed from the circulation by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

J01C A04- Penicillin with extended spectrum
Amoxicillin is a broad spectrum antibiotic.
It is rapidly bactericidal and possesses the safety profile of a penicillin.
The wide range of organisms sensitive to the bactericidal action of Amoxicillin include:

Aerobes:

Gram-positive	**Gram-negative**
Streptococcus faecalis	*Haemophilus influenzae*
Streptococcus pneumoniae	*Escherichia coli*
Streptococcus pyogenes	*Proteus mirabilis*
Streptococcus viridans	*Salmonella* species
Staphylococcus aureus	*Shigella* species
(penicillin-sensitive strains only)	*Bordetella pertussis*
	Brucella species
Corynebacterium species	*Neisseria gonorrhoeae*
Bacillus anthracis	*Neisseria meningitidis*
Listeria monocytogenes	*Vibrio cholerae*
	Pasteurella septica

Anaerobes:
Clostridium species

5.2 Pharmacokinetic properties

Amoxicillin is well absorbed by the oral and parenteral routes. Oral administration, usually at convenient t.d.s. dosage, produces high serum levels independent of the time at which food is taken. Amoxicillin gives good penetration into bronchial secretions and high urinary concentrations of unchanged antibiotic.

In preterm infants with gestational age between 26-33 weeks, the total body clearance after intravenous dosing of amoxicillin, day 3 of life, ranged between 0.75 – 2 ml/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

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium stearate

Capsule Shell:

Gelatin

Sunset Yellow (E110)

Carmoisine (E122)

Brilliant Blue (E133)

Quinoline Yellow (E104)

Titanium Dioxide (E171)

Methylparaben

Propylparaben

6.2 Incompatibilities

None known

6.3 Shelf life

A1/PVC blister packs: 48 months

Securitainers/Bulk container: 36 months

6.4 Special precautions for storage

Store in a dry place below 25°C.

6.5 Nature and contents of container

Securitainers of 100, 250, 500 and 1000 capsules.

Bulk supply of 5,000 and 10,000 capsules packed in polybags, free from additives, inside a cardboard outer container.

A1/PVC blister packs enclosed in an outer carton containing 21 or 100 capsules.

6.6 Special precautions for disposal

Not applicable

7 MARKETING AUTHORISATION HOLDER

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