SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Amoxicillin 250 mg Capsules BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 250 mg Amoxicillin (as trihydrate).

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard.

Red/buff size 2 hard gelatin capsule containing a white to off white powder. Printed with “AMOXY 250”

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of 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
Osteomyelitis
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

Posology

Treatment of infection.

Adults dosage (including the elderly patients)

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

High dose therapy: 3g twice daily is recommended in appropriate cases for the treatment of severe or recurrent purulent infection of the respiratory tract (max daily dose 6g).

Short course therapy: Simple acuteurinary tract infection : two 3g doses with 10-12 hours between the 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 40mg daily, Amoxicillin750mg-1G BID, Metronidazole 400mg
TID x 7 days

Children weighing < 40 kg
For these patients it is more appropriate to use the paediatric presentation, Amoxicillin Oral Suspension.

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.

Renal impairment in children under 40 kg:

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, 750 mg 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 14-21days.

Prophylaxis for endocarditis:

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.

Condition		**Adults' dosage (including elderly)**	**Children's Dosage (< 40 kg)**	**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.	50 mg 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% lidocaime 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 heart valve. c) Patients who have had one or more		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 procedure. Followed by (6	50 mg Amoxicillin/ kg body weight given as a single dose one hour preceding 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 sheet for full prescribing information on

attacks of endocarditis.		hours later): 500 mg Amoxicillin orally.		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.	50 mg 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/DF.
	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.	50 mg Amoxicillin/ kg body weight given as a single dose one hour preceding the surgical procedure	See Notes 2, 3, 4 and 5 above.

Method of administration:
For oral use

4.3 Contraindications

Amoxicillin is a penicillin and should not be given to patients that have hypersensitivity to penicillin's or to any of the excipients. Attention should be paid to possible cross-sensitivity with other beta lactam antibiotics e.g. cephalosporin.

Before initiating therapy with Amoxicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillin's, cephalosporin's.

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

4.4 Special warnings and precautions for use

The capsule shell colours sunset yellow (E110) and carmoisine (E122) may cause allergic reactions.

The capsule shell contains propyl parahydroxybenzoate (E216) and methyl parahydroxybenzoate (E218) which may cause allergic reactions (possibly delayed).

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).

Use with caution in patients with acute and chronic lymphocytic leukaemia.

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

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).

4.5 Interaction with other medicinal products and other forms of interaction

The incidence of allergic skin reactions with Amoxicillin is increased by concomitant allopurinol.

The excretion of methotrexate can be markedly reduced by concurrent use of penicillins. There is considerable risk of methotrexate toxicity.

Very infrequently and unpredictably concurrent use with oral contraceptives may result in contraceptive failure. In common with other antibiotics, Amoxicillin may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

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

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

Breast-feeding:
Amoxicillin may be given during lactation, with the exception of the risk of sensitisation associated with the excretion of trace quantities of Amoxicillin can be detected in breast milk there are no known detrimental effects for the breast-fed infant.

4.7 Effects on ability to drive and use machines

This medicine may very rarely cause dizziness and convulsions. If affected do not drive or operate machinery.

4.8 Undesirable effects

There are no modern clinical studies available that can be used to determine the frequency of undesirable effects.

The following convention has been utilised for the classification of frequency: Very common, ≥ 1/10; common, ≥ 1/100 and < 1/10; uncommon, ≥ 1/1000 and < 1/100; rare, ≥ 1/10000 and < 1/1000; very rare, < 1/10000.

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 has been derived from more than 30 years of post-marketing reports.

System Organ Class	**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	**Frequency not known** (cannot be estimated from available data)
Infections & Infestations				Mucocutaneous candidiasis.	
Blood and lymphatic system disorders:				Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia. Prolongation of bleeding time and prothrombin. (see section 4.4 – Special Warnings and Precautions for Use)	
Immune system disorders:				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. If a hypersensitivity	

				reaction is reported, the treatment must be discontinued. (See also Skin and subcutaneous tissue disorders).	
Nervous system disorders:				Hyperkinesia, dizziness and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses	
Gastrointestinal disorders:	*Clinical Trial Data: Diarrhoea; indigestion; nausea.	*Clinical Trial Data: Vomiting.		Post-marketing Data: 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.	
<u>Hepato-biliary disorders:</u>				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:Skin rash	Clinical Trial Data:Urticaria and pruritus		Post-marketing Data: 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 & urinary disorders:				Interstitial nephritis. Crystalluria (see Section 4.9 Overdose)	

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

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

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).

Overdosage is unlikely but gross overdosage will result in very high urinary concentrations. Problems occurring as a result of this are unlikely if adequate fluid intake and urinary output are maintained, however, crystalluria is a possibility. More specific measures may be necessary in patients with impaired renal function.

Amoxicillin may be removed from the circulation by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Penicillins with extended spectrum. ATC code: JO1C A04

Mechanism of action:

Amoxicillin is a penicillinase-susceptible semisynthetic penicillin. The drug is bactericidal and is effective against the same range of organisms as ampicillin and has a similar mode of action. It has been reported that amoxicillin predominantly inhibits cell-wall synthesis in susceptible bacteria. Amoxicillin has been reported to be slightly more active than ampicillin against some streptococci and salmonella sp. but less active against shigella sp.

The wide range of organisms sensitive to the bactericidal action of Amoxicillin include:

Aerobes:

Gram-positive	Gram-negative
Streptococcus faecalis	*Haemophilus influenzae*
Streptococcus pneumonia	*Escherichia coli*
Streptococcus pyogenes	*Proteus mirabilis*
Streptococcus viridians	*Salmonella* species
Staphylococcus aureus (penicillin-sensitive strains only)	*Shigella* species
	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

Absorption
Amoxicillin is more rapidly and completely absorbed from the GI tract than ampicillin and peak plasma levels are 2-2.5 times greater for amoxicillin after oral administration of the same dose. Food does not interfere with absorption. MIC's ranging from 0.01 to 5 µg/ml have been reported.

The bioavailability of amoxicillin capsules 250 mg and 500 mg was compared against that of Amoxil capsules 250 mg and 500 mg (manufactured by Smithkline Beecham). The results showed that Amoxicillin Capsules 250 mg and 500 mg were bio-equivalent to Amoxil 250 mg and 500 mg respectively.

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

Elimination

In preterm infants with gestational age 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 inuline clearance (GFR) in this population.

Oral bioavailability of Amoxicillin	= 93 ±10%
Urinary excretion of Amoxicillin	= 52 ±15%
Plasma binding	18%
Half life	1 hour (increased in uraemia)

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
No data of relevance, which is additional to that already, included in other sections of the SPC.

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)
Methyl Parahydroxybenzoate (E218)
Propyl Parahydroxybenzoate (E216)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years.

6.4 Special precautions for storage

Tablet container: Do not store above 25°C. Keep the container tightly closed.

Bag: Do not store above 25°C. Keep the container tightly closed.

Blister: Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

PP or HDPE tablet containers with PP or HDPE caps containing 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.

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

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special instructions for use/handling.

7 MARKETING AUTHORISATION HOLDER

Special Concept Development (UK) Ltd
Units 1-7 Colonial Way
Watford
Hertfordshire
WD24 4YR

8 MARKETING AUTHORISATION NUMBER(S)

PL 36722/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04/02/2009

10 DATE OF REVISION OF THE TEXT

13/05/2016