Summary of Product Characteristics

1. Name of the medicinal product

Amoxicillin capsule 250mg/500mg

2. Qualitative and quantitative composition

Amoxicillin capsule 250mg

Each capsule contains amoxicillin trihydrate 287mg equivalent to amoxicillin 250mg.

Amoxicillin capsule 500mg

Each capsule contains amoxicillin trihydrate 574mg equivalent to amoxicillin 500mg.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Capsule

White or almost white crystalline powder or granule in hard gelatine capsules

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

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 organisms 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-dosage therapy (maximum recommended oral dosage 6 g daily in divided doses): A dosage of 3 g 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 3 g doses with 10-12 hours between the doses. Dental abscess: two 3 g doses with 8 hours between the doses. Gonorrhoea: single 3 g 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:

Glomerular filtration rate>30ml/min No adjustment necessary.

Glomerular filtration rate 10-30ml/min: Amoxicillin. max.250 / 500MGb.d

Glomerular filtration rate<10ml/min: Amoxicillin. Max. 250mg/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 500 mg BID x 7 days or

Omeprazole 40 mg daily, Amoxicillin 750 mg -1G BID, Metronidazole 400 mg TID x 7 days.

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.

* 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 of endocarditis: see table on next page.
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.
Prophylaxis of endocarditis

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.)	Patients 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 antibiotic are recommended if more frequent prophylaxis, 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 antibiotic 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 attacks of endocarditis.		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 hours later): 500 mg Amoxicillin orally	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 gentamicin.
Genito-urinary Surgery or Instrumentation: Prophylaxis for patients who have no urinary tract infection and who are to have genitourinary surgery or instrumentation under general anaesthesia. In the case of Obstetric and Gynaecological Procedures and Gastro-intestinal 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	50 mg amoxicillin/kg body weight given as a single dose one	See Note 2 above. Note 5. The second dose of Amoxicillin may be

		Amoxicillin IV or IM 6 hours later.	hour preceding the surgical procedure	administered orally as Amoxicillin Syrup.
	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.

4.3 Contraindications

Amoxicillin is a penicillin and should not be given to penicillin-hypersensitive patients. Attention should be given 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.

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.

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.

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.

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 antibiotics, amoxicillin may affect the gut flora, leading to lower oestrogen reabsorption and reduce efficacy of combined oral contraceptives.
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.
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

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 sensitization 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 is 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.
Immune system disorders	
Very rare:	As with other antibiotics, severe allergic reactions, including angioneurotic oedema, anaphylaxis, serum sickness and hypersensitivity vasculitis. If a hypersensitivity reaction is reported, the treatment must be discontinued.
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:	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 generalized exanthematous pustulosis (AGEP) (See also Immune system disorders).
Renal and urinary tract disorders	
Very rare:	Interstitial nephritis. Crystalluria

*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

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.
Amoxicillin may be removed from the circulation by haemodialysis.

5.1 Pharmacodynamic properties

Amoxillin 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 Amoxillin include:

Aerobes:

Gram-positive	Gram-negative
Streptococcus faecalis	Haemophilus influenzae

Streptococcus pneumoniae
Streptococcus pyogenes
Streptococcus viridans
Staphylococcus aureus
(penicillin-sensitive strains only)

Corynebacterium species
Bacillus anthracis
Listeria monocytogenes

Escherichia coli
Proteus mirabilis
Salmonella species
Shigella species
Bordetella pertussis
Brucella species
Neisseria gonorrhoeae
Neisseria meningitidis
Vibrio cholerae
Pasteurella septica

Anaerobes:
Clostridium species

5.2 Pharmacokinetic properties

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

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. 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
Purified talc

6. 2 Incompatibilities

None known.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 30°C. Protect from light and moisture.

6.5 Nature and contents of container

10 capsules/blister, 10 blisters/box, 100 boxes/carton

6.6 Special precautions for disposal and other handling

Not applicable.

7. Marketing authorisation holder
Guilin Pharmaceutical (Shanghai) Co., Ltd.
Manufacturer
Reyoung Pharmaceutical Co., Ltd.
No. 1, Ruiyang Road, Yiyuan County, Shandong Province, China.

8. Marketing authorisation number(s)
N/A.

9. Date of first authorisation/renewal of the authorisation
N/A.

10. Date of revision of the text
May, 2017.