SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Amoxicillin Sodium for Injection BP 250mg
Amoxicillin Sodium for Injection BP 500mg
Amoxicillin Sodium for Injection BP 1g

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium Amoxicillin equivalent to Amoxicillin Ph Eur 250mg
Sodium Amoxicillin equivalent to Amoxicillin Ph Eur 500mg
Sodium Amoxicillin equivalent to Amoxicillin Ph Eur 1g

3. PHARMACEUTICAL FORM

Powder for solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Amoxicillin is a broad-spectrum aminopenicillin and is indicated in the treatment of bacterial infections such as actinomycosis, biliary-tract infections, bone and joint infections, acute exacerbations of chronic bronchitis, gastroenteritis, (including *Escherichia coli* enteritis and *Salmonella* enteritis, but not shigellosis), gonorrhoea, mouth infections, sinusitis, otitis media, pneumonia (except where *Mycoplasma*suspected), typhoid and paratyphoid fever, urinary-tract infections, bacterial meningitis and the prophylaxis of endocarditis.

It is also used in the treatment of Lyme disease.

4.2 Posology and method of administration

Treatment of Infections in Adults and the Elderly

By intramuscular injection: 500mg every eight hours.

By intravenous injection or infusion:	500mg every eight hours (or in severe infection 1g every six hours) may be given by slow iv injection over three to four minutes or by infusion over 30 to 60 minutes.

Treatment of Infection in Children up to 10 years

By intramuscular or intravenous injection or infusion:	50-100mg per kg bodyweight daily in divided doses.

Renal impairment

It may be necessary to reduce the total daily dosage depending on the degree of renal impairment.

As amoxicillin is removed by haemodialysis, patients receiving haemodialysis may require another dose of amoxicillin at the end of their dialysis.

Endocarditis prophylaxis

Dental procedures under general anaesthesia Upper respiratory tract procedures under general anaesthesia:	No special risk (ie, no prosthetic heart valves, no history of endocarditis, not more than a single dose of a penicillin in the previous month)	**Adults and the elderly:** 1g amoxicillin iv at induction, followed by 500mg oral, iv or im amoxicillin six hours later **Children under 5 years:** Quarter adult dose **Children 5-10 years:** Half adult dose
	Special risk (with prosthetic heart valves, history of endocarditis, or receipt of more than a single dose of a penicillin in the previous month)	**Adults and the elderly:** 1g amoxicillin iv with im or iv gentamicin at induction, followed by 500mg oral, iv or im amoxicillin six hours later **Children under 5 years:** Quarter adult dose plus gentamicin **Children 5-10 years:** Half adult dose plus gentamicin *NB Amoxicillin and gentamicin should not be*

		mixed in the same syringe
Genito-urinary procedures under general anaesthesia in patients with no urinary tract infection: Gastrointestinal, obstetric and gynaecological procedures under general anaesthesia for patients with prosthetic heart valves or history of endocarditis:		**Adults and the elderly:** 1g amoxicillin iv with im or iv gentamicin at induction, followed by 500mg oral, iv or im amoxicillin six hours later **Children under 5 years:** Quarter adult dose plus gentamicin **Children 5-10 years:** Half adult dose plus gentamicin NB Amoxicillin and gentamicin should not be mixed in the same syringe

Method of Administration

Intravenous Injection: Dissolve 250mg in 5mL Water for Injections Ph Eur (final volume 5.2mL).
Dissolve 500mg in 10mL Water for Injections Ph Eur (final volume 10.4mL).
Dissolve 1g in 20mL Water for Injections Ph Eur (final volume 20.8mL).

Amoxicillin Sodium for Injection BP, when diluted may be injected slowly into a vein or infusion line over three to four minutes.

Intravenous Infusion:

Prepare as above and add to an iv solution in a minibag or in-line burette. Administer over 30 to 60 minutes. Alternatively the appropriate volume of iv fluid may be transferred from the infusion bag into the vial, using a suitable reconstitution device, and drawn back into the bag after dissolution.

Intramuscular Injection: Add 1.5mL Water for Injections Ph Eur to 250mg and shake vigorously (final volume 1.7mL).
Add 2.5mL Water for Injections Ph Eur to 500mg and shake vigorously (final volume 2.9mL).

4.3 Contraindications

Penicillin hypersensitivity.

Glandular fever and lymphatic lymphoma.

Bacterial resistance to amoxicillin or ampicillin.

4.4 Special warnings and precautions for use

Amoxicillin should be given with caution to patients with a history of allergy, especially to drugs. Desensitisation may be necessary if treatment is essential.

Amoxicillin should not be used in patients with underlying defects of the urinary tract or for long-term treatment of recurrent urinary tract infection, as resistance may develop in the enteric flora.

Care is necessary if very high doses of amoxicillin are given, especially if renal function is poor, because of the risk of nephrotoxicity. The intrathecal route should be avoided. Care is also necessary if large doses of sodium (as amoxicillin sodium) are given to patients with impaired renal function or heart failure. Renal and haematological status should be monitored during prolonged and high-dose therapy.

Care is required when treating some patients with syphilis because of the Jarisch-Herxheimer reaction.

Contact with amoxicillin should be avoided since skin sensitisation may occur.

Amoxicillin should preferably not be given to patients with undiagnosed pharyngitis (who may have mononucleosis) or patients with lymphatic leukaemia or possibly HIV infection who may also be at increased risk of developing skin rashes with amoxicillin.

Amoxicillin sodium 250mg, 500mg and 1g powder for solution for injection contains 0.65mmol (14.9mg), 1.3mmol (29.7mg) and 2.6mmol (59.4mg) of sodium per dose, respectively. To be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Amoxicillin may decrease the efficacy of oestrogen-containing oral contraceptives. Plasma concentrations of amoxicillin are enhanced if probenecid is given concurrently. There is reduced excretion of methotrexate (increased risk of toxicity).

There may be antagonism between amoxicillin and bacteriostatic agents such as chloramphenicol. An increased frequency of skin rashes has been reported in patients receiving amoxicillin together with allopurinol, compared to those receiving amoxicillin alone.

4.6 Pregnancy and lactation

There has been no evidence of a teratogenic effect in animals or untoward effect in humans. When antibiotic therapy is required during pregnancy, Amoxicillin may be considered appropriate.

Trace quantities of amoxicillin can be detected in breast milk.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

The most common adverse effects are sensitivity reactions including urticaria, maculo- papular rashes (often appearing more than seven days after commencing treatment), fever, joint pains and angioedema. Anaphylaxis occasionally occurs and has sometimes been fatal. Late sensitivity reactions may include serum sickness-like reactions, haemolytic anaemia and acute interstitial nephritis.

Other adverse effects are generally associated with large intravenous doses of amoxicillin or impaired renal function. These include transient leucopenia and thrombocytopenia, haemolytic anaemia and neutropenia (which might have some immunological basis); prolongation of bleeding time and defective platelet function; convulsions and other signs of central nervous system toxicity (encephalopathy has been reported following intrathecal administration and can be fatal); electrolyte disturbances due to administration of large amounts of sodium.

Most patients with infectious mononucleosis develop a maculopapular rash when treated with amoxicillin, and patients with other lymphoid disorders such as lymphatic leukaemia also appear to be at higher risk.

Some patients with syphilis may experience a Jarisch-Herxheimer reaction shortly after treatment is started. Symptoms include fever, chills, headache and reaction at the site of lesions. The reaction can be dangerous in cardiovascular syphilis or where there is a serious risk of increased local damage such as with optic atrophy.

Gastrointestinal effects (diarrhoea and nausea) reported with amoxicillin commonly occur after oral administration, not parenteral administration. Pseudomembranous colitis has been reported with most antibiotics.

Erythema multiforme (including Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, hepatitis and cholestatic jaundice have been reported with combined amoxicillin and clavulanic acid therapy.

4.9 Overdose

Symptoms: gross overdosage will produce very high urinary concentrations, particularly after parenteral administration. Problems are unlikely if adequate fluid intake and urinary output are maintained but crystalluria is a possibility.

Treatment: is symptomatic. More specific measures may be necessary in patients with impaired renal function. Amoxicillin is removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Amoxicillin is a member of the penicillin family. The penicillin nucleus consists of a thiazolidine ring connected to a β-lactam ring to which is attached a side-chain. The side-chain determines most of the pharmacological and antibacterial properties of the penicillin in question. In the case of amoxicillin the benzyl ring in the side chain extends the range of antimicrobial activity into the Gram-negative bacteria.

Amoxicillin kills bacteria by interfering with the synthesis of the bacterial cell wall. As a result the bacterial cell wall is weakened, the cell swells and then ruptures. Amoxicillin is readily hydrolysed by the staphylococcal penicillinase. Its spectrum of activity is extended by administration with the beta-lactamase inhibitor clavulanic acid.

5.2 Pharmacokinetic properties

After the equivalent of 500mg intramuscular amoxicillin, given as amoxicillin sodium, the serum level peaks at one hour at approximately 14mg L^{-1}

Amoxicillin is rapidly distributed throughout the body but penetrates the uninflamed meninges poorly. Its distribution into the cerebrospinal fluid is known to be less efficient than that of ampicillin. Amoxicillin concentrations in interstitial fluid peak around one hour after the serum peak, according to skin window tests. Concentrations in umbilical cord blood have been found to be a fraction of those in maternal blood. Concentrations in amniotic fluid are variable but less than 50% of maternal blood levels. The volume of blood distribution is 0.3 Lkg^{-1} bodyweight. Plasma protein binding is around 20%. Only small amounts of the drug are excreted in breast-milk.

Elimination of amoxicillin occurs via the kidneys by glomerular filtration and tubular secretion. After parenteral administration, 75% of the dose is excreted via the kidneys within the following six hours. High concentrations have been recorded in the bile, but in the presence of biliary tract obstruction amoxicillin may be undetectable.

A small amount (10-20%) of the drug is metabolised by hydrolysis of the β-lactam ring to penicilloic acid, which is excreted in the urine. There is limited enterohepatic circulation of the antibiotic.

5.3 Preclinical safety data

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None

6.2 Incompatibilities

If amoxicillin is prescribed concurrently with an aminoglycoside, the antibiotics should not be mixed in the syringe, intravenous fluid container or giving set because under these conditions, loss of activity of the aminoglycoside can occur.

Amoxicillin should not be mixed with blood products or other proteinaceous fluids (eg protein hydrolysates) or with intravenous lipid emulsions.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Seal up, protect from light.

Reconstituted solutions should be administered immediately after preparation.

6.5 Nature and contents of container

Vials containing 250mg or 500mg of amoxicillin sodium for injection in packs of 10 vials. Vials containing 1g of amoxicillin sodium for injection in single packs.

6.6 Special precautions for disposal and other handling

The vials are not suitable for multidose use.

7. MARKETING AUTHORISATION HOLDER

HARBIN PHARMACEUTICAL GROUP CO., LTD

General Pharm. Factory

No.109 Xuefu Road Nangang Dist, Harbin city

People Republic of China

8. MARKETING AUTHORISATION NUMBER(S)

Vials 0.5g H10930109

9. Date of first authorisation/renewal of the authorisation

Oct.14, 2010 (Re-registration date)

10. DATE OF REVISION OF THE TEXT

APR. 2021

LEGAL STATUS

POM