Summary of Product Characteristics

1. Name of the medicinal product

Ampicillin Sodium and Cloxacillin Sodium for Injection 500mg

2. Qualitative and quantitative composition

Each vial contains Ampicillin Sodium equivalent to Ampicillin 250mg, Cloxacillin sodium equivalent to Cloxacillin 250mg

For full list of excipients, see section 6.1

3. Pharmaceutical form

Powder for injection

White or almost white powder or crystalline powder.

4. Clinical particulars

4.1 Therapeutic indications

Ampicillin and Cloxacillin sodium is indicated for the treatment of the following infections including mixed Gram- positive (except methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant coagulase-negative staphylococcus (MRCoNS)) and Gram-negative infections:
Surgery: post-operative wound infections, post-operative pulmonary infections.
Respiratory infections: bronchopneumonia, acute exacerbations of chronic bronchitis.
Obstetrics: puerperal fever.
Other infections such as septicaemia, bone infections e.g., osteomyelitis, ear, nose and throat infections.
Appropriate culture and susceptibility tests should be performed before treatment in order to isolate and identify organisms causing infection and to determine their susceptibility to Ampicillin and Cloxacillin sodium. Where treatment is initiated before results are available expert advice should be sought when the local prevalence of resistance is such that the utility of Ampicillin and Cloxacillin sodium is questionable (see Pharmacological properties, Pharmacodynamics).
Ampicillin and Cloxacillin sodium neonatal oral drops are indicated for the prophylaxis or treatment of bacterial infections in premature babies or neonates, caused by known susceptibile strains of bacteria.

4.2 Posology and method of administration

Route of administration:

Intramuscular, intravenous.

Preparation of solutions:

Pharmaceutical preparation

ADD: No.1 Ruiyang Road, Yiyuan County, Shandong Province, P.R. China.
Tel: 86 533 3227245/3257891 Fax: 86 533 3257886
E-mail: xie.manyi@reyoungh.com Http://www.reyoung.com

Only freshly prepared solutions should be used. Reconstituted solutions of Ampicillin sodium and Cloxacillin sodium are intended for immediate administration.

Dosage and administration:

The doses of Ampicillin sodium and Cloxacillin sodium will depend on the severity of the disease, the age of the patient and their renal function. The dose should be reduced in renal failure. The usual dose of Ampiclox is as follows:

Adult: 500mg to 1g every 6 hourly or more frequently according to severity of infection.

Children: Up to 2 years: 250mg (5ml of syrup) every 6 hours.

Children 2 – 10 years, (5 – 10ml of syrup) every 6 hours

4.3 Contraindications

Ampicillin sodium and Cloxacillin sodium is contraindicated in patients with a history of allergic reactions to penicillins.

4.4 Special warnings and precautions for use

Warnings

This medication contains ampicillin. Do not take Ampi, Omnipen, Penglobe, or Principen if you are allergic to ampicillin or any ingredients contained in this drug

Keep out of reach of children

In case of overdose, get medical help or contact a Poison Control Center immediately

4.5 Interaction with other medicinal products and other forms of interaction

Other Drug Interactions

Failure of oral contraceptives, increased rash with allopurinol, reduced bactericidal activity with chloramphenicol, erythromycin and tetracyclines.

Potentially Fatal: NA.

Other Interactions

Food: Reduced absorption for ampicillin & delayed obsorption for cloxacillin

4.6 Fertility, pregnancy and lactation

Adequate human data on use during pregnancy are not available. However, animal studies have not identified any risk to pregnancy or embryo-foetal development.

Adequate human and animal data on use during lactation are not available.

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effects

The following statements reflect the information available on the adverse reaction profile of the individual constituents (ampicillin and cloxacillin) and/or the combination in Ampicillin and Cloxacillin sodium. The majority of the adverse reactions listed below are not unique to ampicillin - cloxacillin and may occur when using other penicillins.

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: 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), including isolated reports. Common and uncommon adverse reactions were generally determined from pooled safety data from a clinical trial population of 1210 treated patients. Rare and very rare adverse reactions were generally determined from more than 32 years of post-marketing experience data and refer to reporting rate rather than true frequency.

Blood and lymphatic system disorders	
Very rare:	Hemolytic anemia, leucopenia, thrombocytopenia, agranulocytosis
Immune system disorders	

Very rare: Anaphylaxis (See Warnings and Precautions) and other hypersensitivity reactions

Skin disorders and interstitial nephritis have been reported as hypersensitivity reactions. (See also Skin and subcutaneous tissue disorders and Renal and urinary disorders).

If any hypersensitivity reaction occurs, the treatment should be discontinued.

Nervous system disorders

Very rare: Myoclonus and convulsions

Gastrointestinal disorders

Common: Diarrhoea and nausea

Uncommon: Vomiting

Very rare: Pseudomembranous colitis (See Warnings and Precautions) and haemorrhagic colitis

Hepatobiliary disorders

Very rare: Hepatitis and cholestatic jaundice. A moderate and transient increase in transaminases

Skin and subcutaneous tissue disorders

Common: Skin rash, urticaria, and pruritus

The incidence of skin rash, pruritus, and urticaria is higher in patients suffering from infectious mononucleosis and acute or chronic leukaemia of lymphoid origin.

Very rare: Bullous reactions (including erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis), exfoliative dermatitis and purpura

Skin disorders have also been reported as hypersensitivity reactions (See Immune system disorders).

Renal and urinary disorders

Very rare: Interstitial nephritis

Interstitial nephritis has also been reported as a hypersensitivity reaction (See also Immune system disorders).

4.9 Overdose

Excessive blood levels of Ampicillin sodium and Cloxacillin sodium can be corrected by haemodialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Ampicillin and Cloxacillin sodium is a combination of ampicillin and cloxacillin. Cloxacillin is a narrow-spectrum antibiotic of the isoxazolyl penicillin group; it is not inactivated by staphylococcal beta- lactamases. Ampicillin is a broad-spectrum antibiotic of the aminopenicillin group; it is not resistant to beta-lactamases.

Both ampicillin and cloxacillin are bactericidal antibiotics and act by interfering with the formation of new bacterial cell wall by dividing organisms.

The prevalence of acquired resistance is geographically variable and for select species may be very high. Local information on resistance is desirable, particularly when treating severe infections.

Ampicillin and Cloxacillin sodium susceptibility rates are higher than ampicillin rates due to the cloxacillin activity against β-lactamase producing staphylococci. Methicillin-susceptible Staphylococcus aureus (MSSA) and methicillin-susceptible coagulase-negative staphylococcus (MSCoNS) are commonly susceptible to Ampicillin and Cloxacillin sodium. MRSA and MRCoNS are resistant to Ampicillin and Cloxacillin sodium. For all other indicated bacterial species, the susceptibility of Ampicillin and Cloxacillin sodium is similar to ampicillin including limited activity against Gram-negative organisms.

5.2 Pharmacokinetic properties

Absorption

Ampicillin and Cloxacillin sodium can be administered intravenously and intramuscularly, and the drug is completely absorbed.

Distribution

Ampicillin and Cloxacillin sodium diffuses well into most tissues and body fluids including, among others, bronchial secretions, sinuses, saliva, cerebrospinal fluid (variable percentage depending on the degree of meningeal inflammation), bile, serous membranes and middle ear.

Crossing the meningeal barrier: Ampicillin and Cloxacillin sodium diffuses in only small proportion into the cerebrospinal fluid of subjects whose meninges are not inflamed.

Crossing into breast milk: Ampicillin and Cloxacillin sodium is excreted in small quantities in breast milk. Plasma half-life for cloxacillin is 0.5 to 1 hour and 1 to 1.5 hour for ampicillin.

Protein binding: the serum protein binding proportion is approximately 94% for cloxacillin and 18% for ampicillin.

Metabolism

In normal subjects approximately 20% (cloxacillin) and 40% (ampicillin) of the dose administered is metabolised.

Excretion

Ampicillin and Cloxacillin sodium is eliminated mainly through the kidney. Approximately 30% of the dose administered orally and over 60% of the ampicillin dose administered parenterally is eliminated in active form in the urine within 24 hours. The equivalent percentages for cloxacillin are approximately 20% and 30% respectively. A small proportion (10%) of the dose administered is excreted in bile.

5.3 Preclinical safety data

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

6. Pharmaceutical particulars

6.1 List of excipients

None.

6.2 Incompatibilities

Ampicillin and Cloxacillin sodium must not be dissolved in either protein or protein hydrolysate solutions or in lipid solutions, or in blood or plasma.

When Ampicillin and Cloxacillin sodium is prescribed together with an aminoglycoside, the two antibiotics should not be mixed in the same container as the one containing the infusion solution because a loss of activity may occur.

6.3 Shelf life

Unopened 36 months.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

7ml USP type II glass mould vials, non-flip-off cap, 10vials/tray/box, 100boxes/carton

6.6 Special precautions for disposal and other handling

After contact with skin, wash immediately with water. In case of contact with eyes, rinse immediately with plenty of water and seek medical advice if discomfort persists.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Manufacturer

Manufacturer: Reyoung Pharmaceutical Co., Ltd.

Manufacturing site: No.1 RuiYang Road, Yiyuan County, Shandong Province, P.R. China.

ADD: No.1 Ruiyang Road, Yiyuan County, Shandong Province, P.R. China.
Tel: 86 533 3227245/3257891 Fax: 86 533 3257886
E-mail: xie.manyi@reyoungh.com Http://www.reyoung.com