SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. NAME OF THE MEDICIANAL PRODUCT

Kareclox 500mg injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Cloxacillin sodium equivalent to Cloxacillin 500mg per vial

For excipients: Not applicable

3. PHARMACEUTICAL FORM

Powder for solution for injection or infusion.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

The treatment of beta-hemolytic streptococcal and pneumococcal infections as well as staphylococcal infections (including those caused by beta-lactamase producing organisms). In severe staphylococcal infections (septicaemia, osteomyelitis, endocarditis, pneumonia) or when staphylococci are suspected and treatment is required before sensitivity results are available, parenteral Cloxacillin should be administered at once, followed by Cloxacillin orally, when indicated.

It is not effective against the so called “methicillin-resistant” strains of staphylococcus. If the results of identification and susceptibility testing indicate that the infection is due to an organism other than a penicillinase producing staphylococcus susceptible to Cloxacillin sodium, treatment should be discontinued and therapy with an alternative agent instituted.

4.2 Posology and method of administration

Please note: The reconstituted solution must be shaken well before use.
Dosage

Adults – 250 to 500 mg i.m. or i.v. every 6 hours.

Children up to 20 kg – 25 to 50 mg/kg/day into 4 equal doses, administered i.m. or i.v. every 6 hours.

I.V. dosage may be increased in serious infections. Maximum dosage for adults is 6 g/day.

Administration:

I.M./I.V. Use: Shake well to dissolve. Administer total contents of vial by slow infusion over 2 - 4 minutes. Immediate use of the reconstituted solution is recommended.

I.V. Infusion: Shake well to dissolve. Administer total contents of vial by slow infusion over 30 - 40 minutes. Immediate use of the reconstituted solution is recommended.

Powder for injection, in 500 mg vial, to be dissolved in 4 ml of water for injection, for IV infusion in 0.9% sodium chloride or 5% glucose, to be administered in 60 minutes

Reconstituted Solutions:

Use only Sterile Water for Injection. Immediate use of reconstituted solutions is recommended; however reconstituted solutions may be stored for up to 24 hours at controlled room temperature not exceeding 25°C or 48 hours under refrigeration. Products should be reconstituted as directed below and may be added to an appropriate infusion fluid in the amount calculated to give the desired dose.

For I.M. Use: Using Sterile Water for Injection, reconstitute as follows:

Fill Size (mg)	Volume of Diluent Added (mL)	Withdrawable Volume (mL)	Nominal Concentration (mg/mL)
500	1.7	2.0	250

For I.V. Use: Using Sterile Water for Injection, reconstitute as follows:

Fill Size (mg)	Volume of Diluent Added (mL)	Withdrawable Volume (mL)	Nominal Concentration (mg/mL)
500	4.8	5.0	100
1000	9.6	10.0	100

For I.V. Infusion: Using Sterile Water for Injection, reconstitute as follows:

Fill Size (mg)	Volume of Diluent Added (mL)	Withdrawable Volume (mL)	Nominal Concentration (mg/mL)
1000	3.4	4.0	250
2000	6.8	8.0	250

Cloxacillin Sodium for Injection should be reconstituted as described above and added to an appropriate infusion fluid in the amount calculated to give the desired dose.

4.3 Contraindications

Patients with a history of penicillin allergy. Neonates born of mothers sensitive to Penicillin. Patients allergic to cephalosporins may also be allergic to Penicillins. Cloxacillin should not be administered by subconjunctival injection or used as an eye drop.
The intrathecal route should be avoided.

4.4 Special warnings and precautions for use

Warnings

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients receiving penicillin or cephalosporin therapy. These reactions are more apt to occur in individuals with a history of sensitivity to multiple allergens. Careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. If an allergic or anaphylactic reaction occurs, discontinue treatment and administer the usual agents, e.g. antihistamines, pressor amines, corticosteroids.

Precautions:

Candidiasis and other super infections may occur, especially in debilitated and malnourished patients, or those with low resistance to infection due to corticosteroids, immune suppressors or irradiation. If super infection occurs, institute appropriate measures.
During long-term therapy, renal, hepatic and hematopoietic functions should be checked periodically. The passage of any penicillin from blood into brain is facilitated by inflamed meninges and during cardiopulmonary bypass. In the presence of such factors, particularly in renal failure when high serum concentrations can be attained, CNS adverse effects including myoclonia, convulsive seizures and depressed consciousness can be expected. Although this complication has not been reported with Cloxacillin, it should be anticipated.

4.5 Interaction with other medicinal products and other forms of interaction

Do not combine with methotrexate (increased methotrexate toxicity).

4.6 Fertility, Pregnancy and lactation

Pregnant Women: Safety in pregnancy has not yet been established.
Paediatrics: Experience in premature and new born infants is limited. Cautious administration of the drug to such patients and frequent evaluation of organ system function is recommended.

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effect

It may be expected the most common untoward reactions will be related to sensitivity. They are more likely to occur in individuals who have previously demonstrated hypersensitivity to penicillins and cephalosporins and in those with a history of allergy, asthma, hay fever or urticaria. All degrees of hypersensitivity, including fatal anaphylaxis, have been reported with penicillin. Gastrointestinal Disturbances: Nausea, vomiting, epigastric discomfort, flatulence and loose stools have been noted in some patients. Allergic reactions (rash, urticaria) including wheezing and sneezing have been reported. Hematologic Disturbances: Eosinophilia, leukopenia, anemia, thrombocytopenia, thrombocytopenic purpura, neutropenia and agranulocytosis have been reported during therapy with the penicillins. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. Thrombophlebitis has occurred during the course of i.v. therapy. Mildly elevated SGOT levels (less than 100 units) have been reported.

4.9 Overdose

Treatment is likely needed only in patients with severely impaired renal function, since patients with normal kidneys excrete penicillins at a fast rate. No specific treatment can be recommended. In patients with severe allergic reactions, general supportive measures (if the patient is in shock) or symptomatic therapy similar to that applied in all cases of hypersensitivity are recommended.

5.0 PHARMACOLOGICAL PROPERTIES

Cloxacillin exerts a bacterial action against susceptible microorganisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell wall mucopeptides. Cloxacillin demonstrates activity against strains of beta-hemolytic streptococci, pneumococci, penicillin G sensitive staphylococci and, due to its resistance to penicillinase, penicillin G resistant (β-lactamase producing) staphylococci. Cloxacillin displays less intrinsic antibacterial activity and a narrower spectrum than penicillin G

5.2 Pharmacokinetic properties

Cloxacillin is stable in an acid medium and is approximately 50% absorbed orally. After an oral dose of 500mg Cloxacillin, a peak serum level of about 8 micrograms/mL is reached in about 1 hour. The serum level after i.m. Cloxacillin is approximately twice that obtained when the same dose is given orally to fasting adults. Food in the stomach or small intestine reduces absorption and peak serum levels are approximately 50% those obtained after fasting. As with other penicillins, concurrent administration of probenecid enhances the serum concentration.
Once absorbed, approximately 94% are bound to plasma proteins. After oral administration, roughly 20% of the dose is excreted in the urine, together with one or more active metabolites as yet unidentified. The half life of elimination is about 30minutes

5.3 Preclinical safety data

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Not applicable

6.2 Incompatibilities

None known

6.3 Shelf-life

3 years

6.4 Special precautions for storage

Store cool dry place below 30°C out of direct sunlight. Keep medicines out of reach of children.

6.5 Nature and contents of container

50's Glass vial

7. Manufacturer

Reyoung Pharmaceutical Co., Ltd.

No.1, Ruiyang Road,Yiyuan County, Shandong Province