PRESCRIBING INFORMATION

[Pr]Cloxacillin for Injection

Cloxacillin Powder for Solution (as cloxacillin sodium)

500mg powder/vial

1g powder/vial

2g powder/vial

10g powder/vial

STERILE

Antibiotic

SteriMax Inc.
2770 Portland Drive,
Oakville, ON
L6H 6R4

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Non-medicinal Ingredients
IV, IM, IV Infusion	Powder for reconstitution for **injection**	None

INDICATIONS AND CLINICAL USE

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.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cloxacillin for Injection and other antibacterial drugs, Cloxacillin for Injection should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

CONTRAINDICATIONS

Cloxacillin for Injection is contraindicated for use:

- in patients who are hypersensitive to this drug, to penicillin, or to cephalosporins or to any component of the container. For a complete listing, see the Dosage Forms, Composition and Packaging section of the Prescribing Information.

WARNINGS AND PRECAUTIONS

Hematologic:
During long-term therapy, renal, hepatic and hematopoietic functions should be checked periodically.

Hepatic:
During long-term therapy, renal, hepatic and hematopoietic functions should be checked periodically.

Immune:
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 or sensitivity to multiple allergens. Careful inquiry should be made concerning previous hypersensitivity to reactions to penicillins, cephalosporins or other allergens. If allergic or anaphylactic reactions occurs, discontinue treatment and administer the usual agents, e.g. antihistamines, pressor amines, corticosteroids. See Contraindications.

Neurologic:
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 concentration 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.

Sensitivity/Resistance:
Candidiasis and other superinfections may occur, especially in debilitated and malnourished patients, or those with low resistance to infection due to corticosteroids, immunosuppressors or irradiation. If superinfection occurs, institute appropriate measures.

Renal:
During long-term therapy, renal, hepatic and hematopoietic functions should be checked periodically.

Special Populations

Pregnant Women:
Safety in pregnancy has not yet been established.

Paediatrics:
Experience in premature and newborn infants is limited. Cautious administration of the drug to such patients and frequent evaluation of organ system function is recommended.

Susceptibility/Resistance

Development of Drug Resistant Bacteria

Prescribing Cloxacillin for Injection in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and risks the development of resistant organisms.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

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:
Nausea, vomiting, epigastric discomfort, flatulence and loose stools have been noted in some patients.

Hematologic: Eosinophilia, leucopenia, anemia, thrombocytopenia, thrombocytopenic, purpura, neutropenia and agranulocytosis have been reported during therapy with 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 level (less than 100 units) have been reported.

Immune:
Allergic reactions (rash, urticaria) including wheezing and sneezing have been reported.

DRUG INTERACTIONS

Drug-Drug Interactions

Probenecid
As with other penicillins, concurrent administration of probenecid enhances the serum concentration of cloxacillin.

DOSAGE AND ADMINISTRATION

Dosing Considerations:

Preparation and Storage of Parenteral Solution:

Tap vial gently to loosen powder. 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 IM use: Using Sterile Water for Injection, reconstitute as follows:

Fill Size (mg)	Volume of Diluent Added (mL)	Withdrawable Volume (mL)	Nominal Concentration (mg/mL)
250	1.9	2.0	125
500	1.7	2.0	250

For IV Use: Using Sterile Water for Injection, reconstitute as follows:

Fill Size (mg)	Volume of Diluent Added (mL)	Withdrawable Volume (mL)	Nominal Concentration (mg/mL)
250	4.9	5.0	50
500	4.8	5.0	100
1000	9.6	10.0	100

For IV 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
10000	34.0	40.0	250

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

Recommended Dose and Dosage Adjustment:

Adults: 250 to 500 mg 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.

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

Administration:

IM/IV 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.

IV 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.

Dispensing from Pharmacy Bulk Vial: The use of pharmacy bulk vial is restricted to hospitals with a recognized intravenous admixture program. The pharmacy bulk vial is intended for single puncture, multiple dispensing.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Center immediately.

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.

ACTION AND CLINICAL PHARMACOLOGY

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.

Pharmacokinetics

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 30 minutes.

STORAGE AND STABILITY

Store dry powder at controlled room temperature 15-30°C.

Cloxacillin for Injection is compatible at concentrations of 1 and 2 mg/mL up to 12 hours at controlled room temperature not exceeding 25°C in dextrose 5% in water, fructose 10% in water or normal saline, M/6 sodium lactate, Lactated Ringer's invert sugar 10% in water or normal saline.

Reconstituted solution may be stored for up to 24 hours at controlled room temperature not exceeding 25°C **or** in refrigerator at 2°- 8°C (36° - 46°F) for up to 48 hours. Discard unused portion.

DOSAGE FORMS, COMPOSITION AND PACKAGING

How Supplied:

[Pr]Cloxacillin for Injection is supplied as a dry powder in vials containing: 500 mg, 1,000 mg, 2,000 mg, or 10 g of cloxacillin base as the sodium salt.

Each gram of Cloxacillin Sodium for injection contains approximately 50 mg, or approximately 5-7% sodium.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

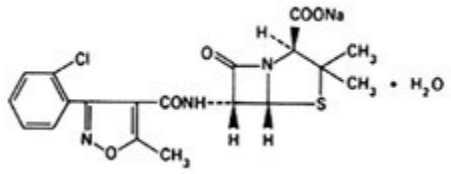
Proper Name: Cloxacillin sodium

Chemical Name: 6-[[[3-(2-Chlorophenyl)-5-methyl-4isoxazolyl[carbonyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, sodium salt

Empirical Formula: $C_{19}H_{17}ClN_3NaO_5S \cdot H_2O$

Molecular Weight: 475.88

Structural Formula:



Physical Characteristics: Cloxacillin sodium is a white, crystalline powder

Solubility: Soluble at 20°C in 2.5 parts water, in 30 parts ethanol (95%) and in 500 parts chloroform.

PART III: CONSUMER INFORMATION

[Pr]Cloxacillin for Injection
Cloxacillin Powder for Solution (as cloxacillin sodium)

This leaflet is Part III of a three-part "Package insert" published when Cloxacillin for Injection was approved for sale in Canada and is designed specifically for Consumers.

This leaflet is a summary and will not tell you everything about Cloxacillin for Injection. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

Cloxacillin for Injection is used to treat streptococcus, pneumonia, and staphylococcus bacterial infections.

Antibacterial drugs like Cloxacillin for Injection treat only bacterial infections. They do not treat viral infections such as the common cold. Although you may feel better early in treatment, Cloxacillin for Injection should be used exactly as directed.

Misuse or overuse of Cloxacillin for Injection could lead to the growth of bacteria that will not be killed by Cloxacillin for Injection (resistance). This means that Cloxacillin for Injection may not work for you in the future. Do not share your medicine.

What it does:

Cloxacillin prevents bacteria from reproducing, which allows your body to fight only the existing bacteria. Cloxacillin for Injection is given intravenously, intramuscularly, or through intravenous infusion.

When it should not be used:

Do not use Cloxacillin for Injection if:

- You are allergic to cloxacillin, penicillin, or cephalosporin medication.

What the medicinal ingredient is:

The medicinal ingredient in Cloxacillin for Injection is cloxacillin, presented as cloxacillin sodium.

What the important nonmedicinal ingredients are:

There are no non-medicinal ingredients. As cloxacillin is presented in its salt form, there are approximately 50mg of sodium per 1g of active ingredient.

What dosage forms it comes in:

Cloxacillin for Injection is available in vials of 500mg, 1g, 2g, and 10 g of cloxacillin as cloxacillin sodium.

WARNINGS AND PRECAUTIONS

BEFORE you use Cloxacillin for Injection talk to your doctor or pharmacist if you have:

- kidney problems
- liver problems
- had allergic reactions before
- been taking corticosteroid medication
- been taking immunosuppressant medication
- or are pregnant or planning a pregnancy

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with Cloxacillin for Injection include:

- Probenecid

Talk to your doctor or pharmacist about any other herbs or vitamin supplements you may be taking.

PROPER USE OF THIS MEDICATION

Usual Dose:
Adults: 200-500mg every 6 hours.

Children (up to 20kg): 25 to 50 mg/kg/day into 4 equal doses every 6 hours.

This dose may be adjusted by your doctor depending on your particular condition and age.

Overdose:
Contact a physician or your Local Poison control center immediately for the management of an overdose even if there are no symptoms.

Missed Dose:
Consult your doctor if you miss a dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Cloxacillin for Injection may cause some side effects such as nausea, vomiting, gastrointestinal discomfort, gas, and diarrhea.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency medical attention
		Only if severe	In all cases	
Rare	Allergic reaction (including skin redness, rash, sneezing, swelling and trouble breathing)			✓
	Weakness, weight loss, general malaise (due to problems with white or red blood cells)			✓

This is not a complete list of side effects. For any unexpected effects while taking Cloxacillin for Injection contact your doctor or pharmacist.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
  Health Canada
  Postal Locator 0701E
  Ottawa, Ontario
  K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

HOW TO STORE IT

Store Cloxacillin for Injection at controlled room temperature (15° - 30°C).

MORE INFORMATION

This document plus the full Prescribing Information, prepared for health professionals can be obtained by contacting the sponsor, SteriMax Inc. at: 1-800-881-3550.

This leaflet was prepared by SteriMax Inc.

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