Sterile

[Pr]Cloxacillin Sodium for Injection, BP

Antibiotic

Actions 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.

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). It is not effective against the so-called "methicillin-resistant" strains of staphylococcus. In severe staphylococcal infections (septicemia, 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. 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.

Contraindications:

A history of allergic reactions to penicillin or cephalosporins.

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 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.

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.

Use in Children:

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.

Use in Pregnancy:

Safety in pregnancy has not been established.

Adverse Effects:

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.

Symptoms and Treatment of Overdosage:
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.

Dosage and Administration:

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.

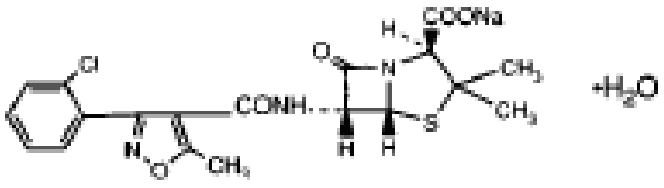
Pharmaceutical Information

Drug Substance:

Name – cloxacillin sodium

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

Structural Formula



Molecular Formula – $C_{19}H_{17}ClN_3NaO_5S \cdot H_2O$

Molecular Weight – 475.88

Description – Cloxacillin sodium is a white, crystalline powder soluble at 20°C in 2.5 parts water, in 30 parts ethanol (95%) and in 500 parts of chloroform.

Composition:

Each vial contains 500 mg, 1000 mg or 2000 mg of cloxacillin base as the sodium salt. Each gram of Cloxacillin Sodium for Injection contains approximately 50 mg, or approximately 5 - 7% sodium.

Stability and Storage Recommendations:

Store dry powder at controlled room temperature not exceeding 25°C.

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.

Parenteral Products:

Cloxacillin 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.

Availability of Dosage Forms:

Cloxacillin Sodium for Injection is supplied as a dry powder in vials containing: 500 mg, 1000 mg or 2000 mg of cloxacillin base as the sodium salt.

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 0701D
  Ottawa, ON 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.

This document plus the full product monograph, prepared for health professionals can be found by contacting Teva Canada Limited at:
1-800-268-4127 ext. 2155005 (English);
1-877-777-9117 (French)
or druginfo@tevacanada.com

This leaflet was prepared by:
Teva Canada Limited
30 Novopharm Court
Toronto, Ontario
Canada, M1B 2K9

Last revised: August 2013