December 2023

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. NAME OF THE MEDICINAL PRODUCT

CLODAX 500 (Cloxacillin 500 mg Capsules)

2. QUALITY AND QUANTITATIVE COMPOSITION

Each hard gelatin capsule contains cloxacillin sodium equivalent to 500mg Cloxacillin

Empty hard gelatin capsules contains approved colours

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule

Hard gelatin capsule having grey coloured cap and yellow coloured body containing white powder within it.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications:

Cloxacillin sodium finds use in the treatment of infections caused by streptococci when associated with sensitive penicillinase-producing staphylococci; also in the treatment of all staphylococcal infections, whether penicillin G-sensitive or resistant.
In infections suspected of being caused by penicillinase-producing staphylococci, cloxacillin may be used for initial treatment after appropriate specimens have been taken for culture and before results of microbial susceptibility tests are known. If the results of identification and susceptibility tests indicate that the infecting organism is not a penicillinase-producing staphylococcus susceptible to cloxacillin, cloxacillin should be discontinued and treatment with an appropriate alternative agent instituted.
To reduce the development of drug-resistant bacteria and maintain the effectiveness of Cloxacillin sodium and other antibacterial drugs, Cloxacillin sodium 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.

4.2 Posology and method of administration:

Posology

Usual Adult Dose for Upper Respiratory Tract Infection

250 mg orally every 6 hours for 7 to 14 days, depending on the nature and severity of the infection.

Maximum dose: 4 g/day.

Usual Adult Dose for Pneumonia

500 mg orally every 6 hours for up to 21 days, depending on the nature and severity of the infection.

Maximum dose: 4 g/day.

Usual Adult Dose for Skin and Structure Infection

500 mg orally every 6 hours for 7 days, or until 3 days after acute inflammation resolves, depending on the nature and severity of the infection.

Maximum dose: 4 g/day.

Usual Adult Dose for Cystitis

250 mg orally every 6 hours for 3 to 7 days, depending on the nature and severity of the infection. Cloxacillin is rarely indicated for the treatment of cystitis.

Maximum dose: 4 g/day.

Usual Pediatric Dose for Pneumonia

The safety and efficacy of cloxacillin in children < 1 year have not been established.

>= 1 year to 18 years: 50 to 100 mg/kg/day orally divided every 6 hours.

Maximum dose: 4 g/day.

Usual Pediatric Dose for Upper Respiratory Tract Infection

The safety and efficacy of cloxacillin in children < 1 year have not been established.

>= 1 year to 18 years: 50 to 100 mg/kg/day orally divided every 6 hours.

Maximum dose: 4 g/day.

Usual Pediatric Dose for Skin and Structure Infection

The safety and efficacy of cloxacillin in children < 1 year have not been established.

>= 1 year to 18 years: 50 to 100 mg/kg/day orally divided every 6 hours.

Maximum dose: 4 g/day.

4.3 Contraindications

Cloxacillin sodium capsules are contraindicated in persons who have shown hypersensitivity to any of the penicillins or any component of the formulations.

4.4 Special warning and precautions for use:

Serious and occasionally fatal hypersensitivity (anaphylactic shock with collapse) reactions have occurred in patients receiving penicillin. The incidence of anaphylactic shock in all penicillin-treated patients is between 0.015% and 0.04%. Anaphylactic shock resulting in death has occurred in approximately 0.002% of the patients treated. Although anaphylaxis is more frequent following a parenteral administration, it has occurred in patients receiving oral penicillins.

When penicillin therapy is indicated, it should be initiated only after a comprehensive patient drug and allergy history has been obtained. If an allergic reaction occurs, Cloxacillin should be discontinued and appropriate therapy instituted. Individuals with a history of penicillin hypersensitivity may also experience allergic reactions when treated with a cephalosporin.

Clostridium difficile associated diarrhea (COAD) has been reported with use of nearly all antibacterial agents, including cloxacillin sodium, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.

C. difficile produces toxins A and B which contribute to the development of COAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. COAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since COAD has been reported to occur over two months after the administration of antibacterial agents.

If COAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

4.5 Interaction with other medicinal products and other forms of interaction

There may be an interaction between cloxacillin and any of the following:

- aminoglycosides (e.g., gentamicin, tobramycin)
- birth control pills
- methotrexate
- tetracyclines (e.g., minocycline, doxycycline)
- typhoid vaccine
- warfarin

If you are taking any of these medications, speak with your doctor or pharmacist. Depending on your specific circumstances, your doctor may want you to:

- stop taking one of the medications,
- change one of the medications to another,
- change how you are taking one or both of the medications, or
- leave everything as is.

An interaction between two medications does not always mean that you must stop taking one of them. Speak to your doctor about how any drug interactions are being managed or should be managed.

Medications other than those listed above may interact with this medication. Tell your doctor or prescriber about all prescription, over-the-counter (non-prescription), and herbal medications you are taking. Also tell them about any supplements you take. Since caffeine, alcohol, the nicotine from cigarettes, or street drugs can affect the action of many medications, you should let your prescriber know if you use them.

4.6 Pregnancy and lactation

Pregnancy:
Reproduction studies performed in the mouse, rat and rabbit have revealed no evidence of impaired fertility or harm to the fetus due to the penicillinase-resistant penicillins. Human experience with the penicillins during pregnancy has not shown any positive evidence of adverse effects on the fetus. There are, however, no adequate or well-controlled studies in pregnant women showing conclusively that harmful effects of these drugs on the fetus can be excluded. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Lactation:
Penicillins are excreted in breast milk. Caution should be exercised when penicillins are administered to a nursing woman.

4.7 Effects on ability to drive and use Machines:

Adverse effects on the ability to drive or operate machinery have not been observed.

4.8 Undesirable effects:

Gastrointestinal

Common gastrointestinal complaints include nausea, vomiting, and diarrhea. Rarely the use of cloxacillin has been associated with pseudomembranous colitis.

Hematologic

Hematologic adverse effects include neutropenia, leukopenia, and thrombocytopenia. Neutropenia has occurred in 17% of patients and occurs most commonly with higher doses and longer durations of therapy. Neutropenia occurs most often after 14 days of therapy and is reversible upon discontinuation.

Hepatic

Hepatic side effects include transient increases in serum transaminases and the development of cholestatic hepatitis. Liver transaminases may take several weeks to return to normal following discontinuation of therapy. Frequent monitoring of liver function tests is recommended in patients with liver disease.

Hypersensitivity

Hypersensitivity reactions include rash, fever, eosinophilia, pruritus, fever, chills, and myalgias.

4.9 Overdose:

When penicillin reaches a certain (as yet undetermined) concentration in the cerebrospinal fluid, neurotoxic symptoms may occur consisting of myoclonia, convulsive seizures, and depressed consciousness. Unless administration of the drug is stopped or its dosage reduced, the syndrome may progress to coma and death. Penicillin does not normally cross the blood-brain barrier to any substantial extent, but when massive doses are used (several grams a day) in the presence of inflamed meninges and/or impaired renal function, or in elderly patients, the drug may cause the above- mentioned toxic reactions. No antidote is required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic Group: Beta-Lactamase Resistant Penicillins

ATC code: J01C F02

Mechanism of Action
Penicillinase-resistant penicillins exert a bactericidal action against penicillin-susceptible microorganisms during the state of active multiplication. All penicillins inhibit the biosynthesis of the bacterial cell wall.

5.2 Pharmacokinetic Properties

Sodium cloxacillin monohydrate is rapidly but incompletely absorbed from the gastrointestinal tract after oral administration.

When a dose of 500 mg cloxacillin sodium (2 x 250 mg cloxacillin sodium capsules) was administered to fasting adult volunteers a mean peak plasma level of 8.5 mcg/mL was obtained with a Tmax of 0.88 hr.
A dose of 500 mg cloxacillin sodium reconstituted granules for oral solution yielded peak plasma levels of 13.3 mcg/mL with a Tmax of 0.58 hr. in fasting adult volunteers.
Oral doses of 250 mg sodium cloxacillin to adult fasting volunteers resulted in 4.8 mcg/mL peak serum levels with a Tmax of 1 hr.
Mean urinary excretion of cloxacillin after an oral dose of 500 mg was found to be 37%.8 Total urinary excretion in healthy volunteers was 62% of an intravenously injected dose of 750 mg
(250 mg/hr for three hours).
Food delays the absorption of cloxacillin sodium. cloxacillin.Sodium cloxacillin is bound to serum proteins to the extent of 94%.
The plasma half-life of cloxacillin is reported to be 25 minutes in healthy volunteers following infusion of 750 mg over a 3 hour period.The plasma half-life in uremic patients was increased to 49 minutes.
Cloxacillin passage across the CNS barrier is insufficient for practical purposes unless the meninges are inflamed. Cloxacillin passes the placental barrier as do the penicillins to the extent of about 50% of the mothers plasma level.
Serum concentrations are enhanced if probenecid is given concomitantly.

5.3 Preclinical safety data

No further information of relevance to add.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Magnesium Stearate BP

Hydrophobic colloidal Anhydrous Silica BP

Sodium Lauryl Sulfate BP

Light liquid paraffin BP

Purified Talc BP

E.H.G Capsule Gray/Yellow, Size “0” Plain IHS

6.2 Incompatibilities:

None stated

6.3 Shelf life:

24 Months

6.4 Special precautions for storage:

Store below 30°C in a cool, dry, and dark place.

6.5 Nature and contents of container:

Primary Packing: 10 tablets of Aluminum Strip and PVDC

Secondary Packing: Such 10 Strip to be packed in a carton along with pack insert. Proposed restriction on sale or distribution.

6.6 Special Precaution for Disposal and other handling:

Nothing stated

7. MARKETING AUTHORIZATION HOLDER

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8. MARKETING AUTHORIZATION NUMBER

08339/09746/NMR/2022

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

03/01/2023

10. DATE OF REVISION OF THE TEXT

04/07/2023

11. REFERENCES