Summary of Product Characteristics

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1. NAME OF THE MEDICINAL PRODUCT

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Cloxacillin Sodium Capsules USP 500 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains

Cloxacillin Sodium USP

Eq. to Cloxacillin 500 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Capsules

Red/White coloured hard gelatin capsule shells of size "O" containing white to off white granular powder

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Cloxacillin is indicated for the treatment of infections due to penicillinase-producing staphylococci that are resistant to benzylpenicillin. It is used against gram-positive staphylococcus aureus in:

- skin and soft tissue infections, e.g. abscesses, cellulitis.
- pneumonia
- endocarditis
- osteomyelitis

4.2 Posology and Method of administration

Children >1 month (<20 kg): 50-100 mg/kg/day in divided doses every 6 hours; up to a maximum of 4 g/day

Children (>20 kg) and Adults: 250-500 mg every 6 hours

Oral: route of administration

4.3 Contraindications

- Cloxacillin should not be given to patients with a history of penicillin allergy or administered to neonates born of mothers hypersensitive to penicillin.
- Patients allergic to cephalosporins may also be allergic to penicillins.
- Cloxacillin is incompatible with arninoglycosides, tetracyclines, erythromycin and polyrnyxin B.

4.4 Special warnings and precautions for use

Concerns related to adverse effects:

Anaphylactoid/hypersensitivity reactions: Serious and occasionally severe or fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy, especially with a history of beta-lactarn hypersensitivity, history of sensitivity to multiple allergens, or previous IgE-mediated

reactions (eg, anaphylaxis, angioedema, urticaria). Use with caution in: asthmatic patients.

CNS effects: Although not reported with cloxacillin, the transport of penicillins across the blood brain barrier may be enhanced by inflamed meninges or during cardiopulmonary bypass. An increased risk of myoclonia, seizures, or reduced consciousness may be observed in these patients (particularly those with renal failure).

Hematologic effects: Penicillin use has been associated with hematologic disorders (eg, agranulocytosis, neuvopenia, thrombocytopenia) . believed to be a hypersensitivity phenomena. Reactions are most often reversible upon discontinuing therapy.

Superinfection: Prolonged use may result in fungal or bacterial superinfection, including C. difficile-associated diarrhea (COAD) and pseudomembranous colitis; COAD has been observed >2 months postantibiotic treatment.

Disease-related concerns:

Renal impairment: Use with caution in patients with renal impairment; rate of elimination is reduced.

Seizure disorders: Use with caution in patients with a history of seizure disorder; high serum levels, particularly in the presence of renal impairment, may increase risk for seizures

Special populations:

Neonates: May have decreased renal clearance of cloxacillin; frequent evaluation of serum levels and of clinical status for adverse effects as well as frequent dosage adjustments may be necessary in this patient population;

4.5 Interaction with other medicinal products and other forms of interact.

Methotrexate: Penicillins may increase the exposure to methotrexate during concurrent therapy; monitor.

Oral contraceptives: Anecdotal reports suggesting decreased contraceptive efficacy with penicillins have been refuted by more rigorous scientific and clinical data.

Probenecid, disulfiram: May increase levels of penicillins (cloxacillin)

Warfarin: Effects ofwarfarin may be increased

4.6 Fertility, Pregnancy and Lactation

Pregnancy:

Safety in pregnancy has not been established. Cloxacillin passes through the placenta into the fetal circulation. This drug should be used in pregnancy only if clearly needed.

Lactation:

Cloxacillin.is distributed into human milk. Therefore, caution should be exercised when cloxacillin is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

Nausea, diarrhoea, abdominal pain, fever, seizure with extremely high doses and/or renal failure, rash (maculopapular to exfoliative), vomiting, pseudomembranous colitis, vaginitis, eosinophilia, leukopenia, neutropenia, thrombocytopenia, agranulocytosis, anemia. hemolytic anemia, prolonged PT, hepatotoxicity, transient elevated LFTs. hematuria, interstitial nephritis, increased BUN/creatinine, serum sickness-like reactions, hypersensitivity.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via EFDA yellow Card Scheme, online at https://primaryreporting.who-umc.org/ET or toll free call 8482 to Ethiopian food and drug authority (EFDA).

4.9 Overdose

Symptoms: neuromuscular hypersensitivity (agitation, hallucinations, asterixis, encephalopathy, confusion, and seizures) and electrolyte imbalance with potassium or sodium salts, especially in renal failure

Treatment: Hemodialysis may be helpful to aid in the removal of the drug from the blood, otherwise most treatment is supportive or symptom-directed

5.0 Pharmacological Properties

5.1 Pharmacodynamic Properties

Inhibits bacterial cell wall synthesis by binding to one or more of the penicillin-binding proteins (PBPs) which in tum inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell walls, thus inhibiting cell wall biosynthesis. Bacteria eventually lyse due to ongoing activity of cell wall autolytic enzymes (autolysins and murein hydro lases) while cell wall assembly is arrested.

5.2 Pharmacokinetic properties

Absorption: Oral: ~50%

Distribution: Widely to most body fluids and bone; penetration into cells, into eye and across normal meninges is poor; crosses placenta; enters breast milk; inflammation increases amount that crosses blood-brain barrier

Protein binding: 90% to 98%

Metabolism: Extensively hepatic to active and inactive metabolites

Half-life elimination: 0.5-1.5 hours; prolonged with renal impairment and in neonates

Time to peak, serum: 0.5-2 hours

Excretion: Urine and fecesz

5.3 Preclinical safety data

Non Stated

6.0 Pharmaceutical particulars

6.1 List of excipients

Purified Talc, Magnesium Stearate

6.2 Incompatibilities

None reported

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store at temperature not exceeding 30°C in a dry place. Protect from light. Keep out of reach of children.

6.5 Nature and contents of container

10 Capsules packed in Aluminium Foil and claer PVC film and such 10 blisters are packed in a unit carton along with package insert.

6.6 Special precautions for disposal and other handling

None reported

7. Marketing Authorisation Holder

MEDICAMEN BIOTECH LIMITED

SP-1192 A & B, Phase-IV,

Industrial Area, Bhiwadi-301019,

Distt Alwar, Rajasthan India

8. Number(s) in the national register of finished pharmaceutical products

Certificate No: 07657/08394/REN/2022

9. Date of first authorisation/renewal of the authorisation

Aug 8, 2022

10. Date of revision of the text

August 2023