1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

CLOXIN 250 mg CAPSULES

CLOXIN 500 mg CAPSULES

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each CLOXIN 250 mg CAPSULE contains 250 mg cloxacillin as cloxacillin sodium.

Each CLOXIN 500 mg CAPSULE contains 500 mg cloxacillin as cloxacillin sodium.

Sugar free.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsules

CLOXIN 250 mg CAPSULES is a hard gelatin capsule (Size 2) with an opaque orange cap and an opaque white body, containing a white powder. “Cloxin 250” printed on the body and cap in black ink.

CLOXIN 500 mg CAPSULES is a hard gelatin capsule (Size 0 EL) with an opaque orange cap and an opaque white body, containing a white powder. “Cloxin 500” printed on the body and cap in black ink.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

CLOXIN 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

Posology

Capsules

Adults: One 500 mg capsule six hourly, administered one hour before meals.

Children 2 to 10 years: One 250 mg capsule six hourly, administered one hour before meals.

Method of administration

For oral administration.

4.3. Contraindications

CLOXIN is contraindicated in:

- Patients with hypersensitivity to cloxacillin or to any excipients in CLOXIN (see section 6.1).
- Patients with a history of penicillin allergy.
- Neonates born from mothers hypersensitive to penicillin.
- Patients allergic to cephalosporins as they may also be allergic to penicillins.

- Concomitant use with aminoglycosides, tetracyclines, erythromycin and polymyxin B (see section 4.5).

4.4. Special warnings and precautions for use

Before initiating therapy with cloxacillin, as contained in CLOXIN, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam agents (see sections 4.3 and 4.8).

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients on penicillin therapy. Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction (see section 4.8). These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and in atopic individuals. If an allergic reaction occurs, cloxacillin therapy must be discontinued and appropriate alternative therapy instituted.

When administered to a patient with penicillin sensitivity anaphylactic shock may occur (see section 4.3).

Adrenaline, corticosteroids and antihistamines should be used to treat anaphylaxis.

Sensitivity reactions may include skin rashes, angioedema, bronchospasm, serum sickness and anaphylaxis, and sometimes death within minutes.

A generalised sensitivity reaction can develop within a few hours or weeks of commencing treatment, including urticaria, fever, joint pains and eosinophilia. Other allergic reactions include exfoliative dermatitis and other skin reactions, interstitial nephritis and vasculitis.

Haemolytic anaemia, leucopenia, prolonged bleeding time and defective platelet function can occur.

Supra-infection with *C. albicans*, other fungi or organisms resistant to cloxacillin, as contained in CLOXIN, may occur.

Due to the variability in intestinal absorption, oral administration is not a suitable substitute for the parenteral treatment of serious infections.

Care should be taken when administering high doses of cloxacillin, especially to patients with impaired renal function, as there is a risk of neurotoxicity and congestive heart failure.

Disturbance of electrolyte balance may occur following administration of large doses.

Increases in liver enzyme values have been reported.

Renal and haematological systems should be monitored during prolonged and high dose therapy.

Patients with syphilis may exhibit the Jarish-Herxheimer reaction and should therefore also be monitored (see section 4.8).

A skin test for sensitivity may be used to determine those patients most likely to develop allergic reactions to penicillins.

Cloxacillin, as contained in CLOXIN, has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Reduced concentrations in patients with cystic fibrosis have been attributed to enhanced non-renal clearance of cloxacillin, as contained in CLOXIN.

Cloxacillin, as contained in CLOXIN, is not removed by haemodialysis.

4.5. Interaction with other medicines and other forms of interaction

Cloxacillin, as contained in CLOXIN, is incompatible with aminoglycosides, tetracyclines, erythromycin and polymyxin B (see section 4.3).

Cloxacillin, as contained in CLOXIN, may interact with bacteriostatic antibacterials such as chloramphenicol.

The possibility of a prolonged bleeding time should be borne in mind in patients receiving anticoagulants.

Cloxacillin, as contained in CLOXIN, may decrease the efficacy of oral contraceptives.

Cloxacillin, as contained in CLOXIN, may enhance the effects of methotrexate, by decreasing its renal excretion.

Plasma concentrations are enhanced if probenecid is given concomitantly.

4.6. Fertility, pregnancy and lactation

Pregnancy

The safety of CLOXIN in pregnancy has not been established.

Breastfeeding

The safety of CLOXIN in lactation has not been established.

Cloxacillin, as contained in CLOXIN, crosses the placenta and is distributed into breast milk.

4.7. Effects on ability to drive and use machines

The effect on the ability to drive and operate machinery is unknown however care should be taken due to the risk of convulsions.

Patients should not drive, use machinery or perform any tasks that require concentration until they are certain that CLOXIN do not adversely affect their ability to do so safely (see section 4.8).

4.8. Undesirable effects

a) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from available data)
Infections and infestations			Symptoms due to overgrowth of non-susceptible organisms (*Aerobacter aerogenes, Pseudomonas, Candida*, etc.) may appear and then cloxacillin should be discontinued and specific or supportive therapy instituted
Blood and the lymphatic system disorders		Leukopenia, prolonged bleeding time and defective platelet function, neutropenia	Haemolytic anaemia

Immune system disorders		Sensitivity reactions may include skin rashes, angioedema, bronchospasm, serum sickness, anaphylaxis and death. Other allergic reactions include exfoliative dermatitis and interstitial nephritis	A generalised sensitivity reaction can develop including urticaria, fever, joint pains and eosinophilia. Other allergic reactions include other skin reactions and vasculitis
Nervous system disorders		Convulsions and other signs of toxicity to the CNS may occur particularly with intravenous administration or in patients with renal failure. The administration of high doses to children may cause cerebral irritation and convulsions	
Cardiac disorders			Kounis syndrome
Gastrointestinal disorders	A sore mouth or tongue, transient diarrhoea, nausea	Oral administration may produce heartburn	A black hairy tongue, pruritus ani, pseudomembranous colitis

Hepatobiliary disorders		Hepatitis and cholestatic jaundice	Increases in liver enzyme values
Skin and subcutaneous tissue disorders			Erythema multiforme type of rash for up to 15 days after stopping administration, linear IgA disease

b) Description of selected adverse reactions

Care should be taken when treating patients with syphilis, as the Jarisch-Herxheimer reaction may occur shortly after starting treatment. This reaction, manifesting as fever, chills, headache and reactions at the site of the lesion, can be dangerous in cardiovascular syphilis or where there is a serious risk of increased local damage such as optic atrophy.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9. Overdose

Symptoms

Following administration of large doses, disturbance of electrolyte balance may occur. Convulsions and other signs of toxicity to the central nervous system may occur with very high doses, particularly when administered intravenously to patients with renal failure. Nephrotoxicity may occur in patients with diminished renal function.

Treatment

Treatment of overdosage is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category and class: A 20.1.2 Penicillins

Pharmacotherapeutic group: Beta-lactam Antibacterials, Penicillins, Beta-lactamase resistant penicillins

ATC code: J01CF02

Mechanism of action

Cloxacillin is a semi-synthetic penicillin, resistant to penicillinase, and is therefore active against penicillinase-producing staphylococci. Cloxacillin is, in general, less effective against organisms susceptible to benzylpenicillin, such as streptococci, pneumococci and non-penicillinase-producing staphylococci, and is not useful against gram-negative bacteria.

Resistant organisms

Cloxacillin is active against both penicillin-sensitive and penicillin-resistant staphylococci, as well as *Streptococcus pyogenes* and *Streptococcus pneumonia*. However, it is less potent than penicillin G against penicillin-sensitive bacteria and has very little activity against *Enterococcus faecalis* and gram-negative organisms.

5.2. Pharmacokinetic properties

Absorption

Cloxacillin is rapidly but incompletely absorbed from the gastrointestinal tract (30 to 80 %). As absorption is more efficient on an empty stomach, it is ideally administered 1 hour before or 2 hours after meals.

Distribution and biotransformation

Peak concentrations in plasma are attained by 1 hour. It is highly bound to plasma albumin (> 90 %) and is not removed from the circulation to a significant degree by haemodialysis.

Elimination

Cloxacillin is excreted rapidly by the kidneys. Normally, it is excreted in the urine within 6 hours of an oral dose. It is also eliminated in the bile.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Erythrosine (C.I. 45430), gelatin, iron oxide black, magnesium stearate, potassium hydroxide, propylene glycol, shellac, starch maize, sunset yellow (C.I. 15985), titanium dioxide (C.I. 77891).

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store at or below 25 °C. Keep container tightly closed.

Keep in original packaging until required for use.

6.5. Nature and contents of container

CLOXIN 250 mg CAPSULES:

100 capsules are packed in a white opaque polypropylene container with a white opaque low density polyethylene cap.

100 capsules are packed in a high density polyethylene container with a white high density polyethylene cap with an aluminium seal.

CLOXIN 500 mg CAPSULES:

100 capsules are packed in a white opaque polypropylene container with a white opaque linear low density polyethylene cap.

100 capsules are packed in a high-density polyethylene container with a white polypropylene cap with induction liner within the cap.

Not all packs are necessarily marketed.

6.6. Special precautions for disposal and other handling

No special precautions.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

Hotline: 0800 122 912

8. REGISTRATION NUMBERS

CLOXIN 250 mg CAPSULES: N/20.1.2/90

CLOXIN 500 mg CAPSULES: N/20.1.2/91

9. DATE OF FIRST AUTHORISATION

Date of registration:

CLOXIN 250 mg CAPSULES: 19 July 1982

CLOXIN 500 mg CAPSULES: 19 July 1982

10. DATE OF REVISION OF TEXT

30 June 2026

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

Namibia:	NS2
CLOXIN 250 mg CAPSULES:	90/20.1.2/00861
CLOXIN 500 mg CAPSULES:	90/20.1.2/00862