August 3, 2026

Direct Healthcare Professional Communication (DHPC)

Availability of English Package leaflet for Cloxacillin Normon 500 mg powder for solution for injection and infusion EFG and Important Safety Information

Dear Healthcare Professional,

Sada Al Dawa Medical Warehouse Company in agreement with Saudi Food and Drug Authority (SFDA) would like to inform healthcare professionals about the availability of English package leaflet for **Cloxacillin Normon 500 mg powder for solution for injection and infusion EFG** containing cloxacillin sodium 500 mg.

This communication aims to support the safe and appropriate use of imported **Cloxacillin Normon 500 mg** batches distributed to healthcare institutions within the Kingdom of Saudi Arabia.

Summary

- Imported **Cloxacillin Normon 500 mg powder for solution for injection and infusion** packs contain the original package leaflet in English language.
- The Manufacturer's Packaging of **Cloxacillin Normon 500 mg** consists of cartons containing 100 vials each. One English leaflet is included per carton and is not affixed to each vial.
- An English package leaflet provided by the manufacturer is attached for healthcare professional reference.
- Healthcare professionals should review the attached English leaflet before prescribing, dispensing, or administrating.
- Suspected adverse drug reactions should be reported to the SFDA National Pharmacovigilance Center through the Saudi Vigilance System.

Background

Cloxacillin Normon 500 mg powder for solution for injection and infusion EFG is manufactured by NORMON LABORATORIES, SA and marketed in Spain.
According to the approved SPC/package leaflet, **Cloxacillin Normon 500** is indicated:

- Treatment of infections caused by penicillinase-producing staphylococci and other Gram-positive bacteria.
- treatment of respiratory tract infections, skin and soft tissue infections, and bone and joint infections.
- Treatment of Sepsis, Endocarditis and Meningitis.

Due to temporary shortages within governmental healthcare institutions in the Kingdom of Saudi Arabia, the product was imported through an authorized distributor in Spain following SFDA approval procedures.

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The imported batches were distributed through NUPCO warehouses to healthcare institutions across the Kingdom.

As the Original package leaflet enclosed with the imported product is available only one Copy for 100 Package not attached to each vial, an English package leaflet provided by the manufacturer is attached to facilitate safe and appropriate product use by healthcare professionals.

Advice for Healthcare Professionals

- Review the attached English package leaflet before prescribing, dispensing, or administering the product.

Call for Reporting

Healthcare professionals are encouraged to report any suspected adverse drug reactions associated with the use of **Cloxacillin Normon 500 mg powder for solution for injection and infusion EFG** to the Saudi Food and Drug Authority (SFDA) National Pharmacovigilance Center through the Saudi Vigilance System.

SFDA barcode for reporting:

tracking.drug@sfda.gov.sa
Website: https://ade.sfda.gov.sa
Email: npc.drug@sfda.gov.sa
Telephone: 19999

Company Information

NORMON LABORATORIES, SA
Ronda de Valdecarrizo, 6 28760 Tres Cantos Madrid (Spain)
website: - www.notificarRAM.es
Yours sincerely,
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This document is approved by The Executive Directorate of Pharmacovigilance, at Saudi Food and Drug Authority (SFDA).

version 1.0 - approved by SFDA: August 2026

1. NAME OF THE MEDICINE

- Cloxacillin Normon 500 mg powder for solution for injection and infusion EFG
- Cloxacillin Normon 1 g powder for solution for injection and infusion EFG

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of Cloxacillin Normon 500 mg contains 606 mg of cloxacillin (as cloxacillin sodium).
Each vial of Cloxacillin Normon 1g contains 1,212 mg of cloxacillin (as cloxacillin sodium).
Cloxacillin Normon 500 mg contains sodium (26.4 mg)
Cloxacillin Normon 1g contains sodium (52.8 mg)
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cloxacillin Normon 500 mg : Powder for solution for injection and infusion.
Cloxacillin Normon 1 g : Powder for solution for injection and infusion.

4. CLINICAL DATA

4.1. Therapeutic indications

Cloxacillin Normon is indicated for the treatment of the following infections caused by sensitive germs *(* See section 5.1 *)* :

1. Skin and soft tissue infections: furunculosis, infected wounds and burns, cellulitis, and pyomyositis.
2. Mastitis.
3. Osteoarticular infections such as septic arthritis and osteomyelitis.
4. Sepsis.
5. Endocarditis.
6. Meningitis.

Official guidelines regarding bacterial resistance and the appropriate use and prescription of antibiotics should be taken into account.

4.2. Dosage and method of administration

Posology

Cloxacillin Normon 500 mg can be administered intramuscularly or intravenously, and Cloxacillin Normon 1 g intravenously. The dosage depends on the severity of the condition, as well as the age and characteristics of the patient.

- **Adults:**

The recommended dose is 500 mg-1 g every 6-8 hours.

- **Children over 2 years old:**

The recommended dose is 12.5-25 mg/kg of weight every 6-8 hours.

- **Children under 2 years:**

A dose of 6.25-12.5 mg/kg of weight every 6 hours is recommended.
These doses are guidelines and may be increased when the severity of the process requires it.
The duration of treatment depends on the type and severity of the infection and will be determined by the patient's clinical and bacteriological response.
Dosage adjustments may be necessary in patients with impaired renal and/or liver function.
Cloxacillin serum levels do not decrease with hemodialysis or peritoneal dialysis. Therefore, no additional dose is required during dialysis.

Method of administration

Cloxacillin Normon 500 mg:

- Intramuscular.
- Slow direct intravenous (3-4 minutes). Can be administered by continuous intravenous infusion over 60 minutes.

Cloxacillin Normon 1 g:

- Slow direct intravenous (3-4 minutes). Can be administered by continuous intravenous infusion over 60 minutes.

4.3. Contraindications

CLOXACILLIN Normon is contraindicated in patients with known hypersensitivity to penicillins or other beta-lactams.

4.4. Special warnings and precautions for use

Before starting therapy with Cloxacillin Normon, the patient should be screened for a history of hypersensitivity to penicillins and cephalosporins. In patients hypersensitive to cephalosporins, the possibility of cross-allergic reactions should be considered.

Severe and sometimes fatal hypersensitivity reactions (anaphylaxis) have been observed in patients treated with beta-lactam antibiotics. If an allergic reaction occurs, cloxacillin treatment should be discontinued and supportive care should be initiated.

It should be administered with caution in neonates with jaundice.
There is a risk of neurotoxicity, especially when administering high doses in cases of impaired kidney function.
Cloxacillin Normon 500 mg contains 26.4 mg (1.15 mmol) of sodium per vial, equivalent to 1.35% of the maximum daily intake of 2 g of sodium recommended by the WHO for an adult.
Cloxacillin Normon 1,000 mg contains 52.8 mg (2.30 mmol) of sodium per vial, equivalent to 2.71% of the maximum daily intake of 2 g of sodium recommended by the WHO for an adult.
The use of antibiotics, including cloxacillin, can alter the normal flora of the colon with overgrowth of *Clostridium difficile* , whose toxin can trigger a case of pseudomembranous colitis that presents with fever, abdominal pain and diarrhea that may be bloody. Its onset may occur during treatment or weeks after it has ended. Anticholinergics and antiperistaltics can aggravate the patient's condition. Mild cases usually respond to discontinuation of cloxacillin treatment, but moderate to severe cases also require treatment with electrolyte solutions, protein therapy and an antibiotic effective against *C. difficile* .

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

- It should not be administered in conjunction with **bacteriostatic antibiotics** (chloramphenicol, tetracycline, erythromycin or sulfonamides), since these drugs may antagonize its bactericidal action.
- Probenecid decreases the renal tubular secretion of penicillins, resulting in increased serum concentrations of cloxacillin and a prolongation of its elimination half-life **.**
- **Oral contraceptives** : Like all broad-spectrum oral antibiotics, cloxacillin may reduce the effectiveness of oral contraceptives.
- **Analytical interactions** :
  - Cloxacillin sodium produces interference in the determination of the serum concentration of aspartate aminotransferase (AST) by increasing its values.
  - It may interfere with some diagnostic tests such as urine glucose determination with copper sulfate, Coombs test and some tests for protein determination in urine and plasma.

4.6. Fertility, pregnancy and lactation

There are no controlled clinical data on cloxacillin in exposed pregnant women. As with all drugs, administration during pregnancy should only be considered if the expected benefit to the mother outweighs any potential risk to the fetus.
Cloxacillin is excreted in breast milk and therefore caution should be exercised when administered to nursing women.

4.7. Effects on ability to drive and use machines

There is no evidence of effects on the ability to drive or operate machinery.

4.8. Adverse reactions

Hypersensitivity reactions: pruritus, skin rash, urticaria, interstitial nephritis. Other reactions such as angioedema, anaphylaxis (hypotension, bronchospasm), and serum sickness have been reported rarely. Treatment should be discontinued if any hypersensitivity reaction occurs.

- *Gastrointestinal tract disorders* : diarrhea, nausea, and vomiting, which are generally mild and transient and do not require discontinuation of treatment. Persistent diarrhea should raise the possibility of pseudomembranous colitis.
- *Hematological reactions* : Cases of neutropenia and platelet dysfunction have been reported rarely.
- *CNS disorders:* At very high doses, seizures and other signs of central nervous system toxicity may occur, particularly when administered intravenously in patients with renal failure.
- *Liver function test abnormalities:* Transient increases in liver enzyme values, cholestatic jaundice and hepatitis have been reported rarely.
- *Local reactions:* Phlebitis may occur after intravenous administration of this medicine.
- *Other adverse reactions:* oral candidiasis.

Reporting of suspected adverse reactions
It is important to report suspected adverse reactions to the medicinal product after its authorization. This allows for continued monitoring of the medicinal product's benefit/risk balance. Healthcare professionals are encouraged to report any suspected adverse reactions via the Spanish Pharmacovigilance System for Medicinal Products for Human Use: www.notificarRAM.es .

4.9. Overdose

Doses of up to 6 g/day have been well tolerated. Overdose with cloxacillin sodium is unlikely, especially if renal function is normal. If this occurs, treatment should be symptomatic and supportive, as there is no specific antidote.
Cloxacillin sodium cannot be removed by hemodialysis or peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: penicillins resistant to beta-lactamases; ATC code: J01CF02.

Mechanism of action

Cloxacillin is an antibiotic belonging to the beta-lactam family, and more specifically to the isoxazolyl penicillin group.

Cloxacillin has a mechanism of action similar to that of other penicillins. Its bactericidal effect is due to the inhibition of bacterial cell wall synthesis by specifically binding to penicillin-binding proteins (PBPs), which are involved in bacterial cell wall synthesis and cell division.

Endurance

Cloxacillin is resistant to inactivation by most staphylococcal penicillinases and is active against penicillinase-producing *Staphylococcus* spp. strains, which generally confer resistance to other penicillins. However, it is not active against *Staphylococcus* spp. strains carrying the *mec* A gene, encoding the PBP2a protein, which has a low affinity for cloxacillin. The prevalence of these cloxacillin-resistant *Staphylococcus aureus* (MRSA) strains varies between geographical areas and the place of acquisition of the infection (hospital- or community-acquired).

Cut-off points

The minimum inhibitory concentrations (MIC) that define the clinical breakpoints that establish the categorization of microorganisms into sensitive, intermediately

sensitive and resistant to cloxacillin are those shown in the following table (EUCAST v6.0 Clinical Breakpoints valid from 01-01-2016):

Microorganisms	Sensitive (S) (mg/l)	Resistant (R) (mg/l)
Staphylococcus aureus	≤ 2	> 2
Staphylococcus lugdunensis / Staphylococcus saprophyticus	≤ 2	> 2
Coagulase-negative staphylococci	≤ 0.25	> 0.25
Streptococcus groups A, C and G [1]	≤ 0.25	> 0.25

[1] The susceptibility of groups A, C, and G streptococci is inferred from the MICs of benzylpenicillin.

Spectrum of antibacterial activity

The antibacterial spectrum of cloxacillin is limited to Gram-positive bacteria, especially *Staphylococcus* spp., group A, B, C and G streptococci, and certain anaerobic microorganisms (*Clostridium perfringens, Peptostreptococcus* spp.). Cloxacillin is not usually active against Gram-negative microorganisms.

The prevalence of acquired resistance to cloxacillin can vary geographically and over time, so it is important to have information on the local epidemiology of resistance, especially when treating serious infections. When the local prevalence of resistance is such that the drug's usefulness is doubtful, at least in some types of infections, expert opinion should be sought as needed.

Classification of the most frequently involved microorganisms with the greatest clinical relevance according to their sensitivity to cloxacillin are:

Table : Antibacterial spectrum of cloxacillin.

FREQUENTLY SENSITIVE SPECIES
Gram-positive aerobes
Streptococcus pyogenes (group A streptococcus)
Gram-positive anaerobes
Clostridium perfringens
SPECIES IN WHICH ACQUIRED RESISTANCE CAN BE A PROBLEM (Resistance ≥ 10%)
Gram-positive aerobes
Staphylococcus aureus
Coagulase-negative staphylococci
INTRINSICALLY RESISTANT SPECIES
Gram-negative aerobic and anaerobic microorganisms

5.2. Pharmacokinetic properties

Absorption

Following intramuscular injection, peak plasma concentrations are reached after 45 minutes. In adults, they are approximately 15 mg/l after a 500 mg dose.

Distribution

Cloxacillin sodium is widely distributed into most body fluids, including, but not limited to, amniotic fluid, synovial fluid, and bone tissue.

Cloxacillin sodium crosses the placenta and appears in umbilical cord blood and amniotic fluid.

Although it crosses the blood-brain barrier, cloxacillin diffuses to a small extent into the cerebrospinal fluid of subjects whose meninges are not inflamed. Inflammatory conditions generally increase the permeability of the blood-brain barrier to penicillins, and this is also true for cloxacillin sodium.

Cloxacillin is excreted in breast milk and therefore caution should be exercised when administered to nursing women.

Protein binding is very high, around 95-97%. The volume of distribution of cloxacillin sodium is 0.1 l/kg.

Biotransformation

Cloxacillin is partially metabolized to active and inactive metabolites.

Elimination

Cloxacillin sodium is eliminated via the kidneys, through tubular secretion and glomerular filtration. Elimination varies depending on the degree of protein binding. Since renal clearance is reduced in newborns, dosage adjustment may be necessary.

Approximately 30–45% of cloxacillin sodium is excreted unchanged in the urine. Its half-life is 0.5–1.1 hours, increasing in cases of renal dysfunction. Cloxacillin sodium undergoes hepatic biotransformation in 9–22% of cases.

Small amounts are also excreted in feces and bile.

Co-administration with probenecid delays the excretion of cloxacillin sodium.

5.3. Preclinical safety data

The lethal dose LD_{50} of cloxacillin sodium administered intraperitoneally is 1630 ± 112 mg/kg of body weight in rats and 1280 ± 50 mg/kg of body weight in mice. Toxicity studies have shown a wide safety margin between normal therapeutic doses of cloxacillin sodium and toxic doses.

6. PHARMACEUTICAL DATA

6.1. List of excipients

None.

6.2. Incompatibilities

Cloxacillin sodium should not be used in solutions containing protein hydrolysates, lipid suspensions, amino acids, blood, or serum. It is compatible with most commonly used intravenous solutions (saline saline or glucose).

Mixing cloxacillin and aminoglycosides can cause substantial mutual inactivation, so they should not be mixed in the same container for administration.

6.3. Period of validity

The validity period is 3 years.

Cloxacillin Normon is stored between 15°C: 25°C.

After reconstitution, the physicochemical stability of the product reconstituted with water for injections has been demonstrated for up to 6 hours at 25°C and 72 hours at 2-8°C. Physicochemical in-use stability of the solution diluted with sodium chloride 9 mg/ml (0.9%) for injection or glucose 50 mg/ml (5%) in infusion bags or bottles has been demonstrated for 6 hours at 25°C or 48 hours at 2-8°C. From a microbiological point of view, the product should be used immediately. If not used immediately, storage times and conditions prior to use are the responsibility of the user and should normally not be longer than 24 hours at 2-8°C, unless dilution/reconstitution has taken place in controlled and validated aseptic conditions.

6.4. Special storage precautions

Store in original packaging.

For storage conditions of the reconstituted medicinal product, see section 6.3.

6.5. Nature and contents of the container

CLOXACILLIN NORMON 500 mg is presented in a type II glass vial closed with a stopper and sealed with an aluminum cap. The package contains 1 vial and the clinical pack contains 100 vials .

Cloxacillin Normon 1 g is presented in a type II glass vial closed with a stopper and sealed with an aluminum cap. The package contains 1 vial, and the clinical pack contains 100 vials.

6.6. Special precautions for disposal and other handling

Cloxacillin Normon 500 mg:

Reconstitution of the 500 mg vial for intramuscular administration is carried out with 3.5 ml of water for injections.

For intravenous administration, the 500 mg vial is reconstituted with 10 ml of water for injections. Inject slowly over 3-4 minutes.

Administration for infusion:

The reconstituted solution should be diluted in 100 ml of diluent immediately after reconstitution.

Suitable diluents are:

Sodium chloride 9 mg/ml (0.9%) for injection and glucose 50 mg/ml (5%) for infusion.

Before administration, reconstituted and diluted solutions should be visually inspected for particulate matter and discoloration. Only clear, colorless, particle-free solutions should be used.

Disposal of unused medicines and all materials that have been in contact with them should be carried out in accordance with local requirements.

Cloxacillin Normon 1 g:

Reconstitution of the 1 g vial for intravenous administration is carried out by dissolving the contents of the vial in 20 ml of water for injections. Any unused antibiotic solution should be discarded.

Administration for infusion:

The reconstituted solution should be diluted in 100 ml of diluent immediately after reconstitution.

Suitable diluents are:

Sodium chloride 9 mg/ml (0.9%) for injection and glucose 50 mg/ml (5%) for infusion.

Before administration, reconstituted and diluted solutions should be visually inspected for particulate matter and discoloration. Only clear, colorless, particle-free solutions should be used.

Disposal of unused medicines and all materials that have been in contact with them should be carried out in accordance with local requirements.

Appearance of the reconstituted solution :

Colorless or slightly yellow, clear solution.

7. MARKETING AUTHORIZATION HOLDER

NORMON LABORATORIES, SA

Ronda de Valdecarrizo, 6 – 28760 Tres Cantos – Madrid (Spain)

8. MARKETING AUTHORIZATION NUMBER(S)

Cloxacillin Normon 500 mg, Registration No.: 63,637

Cloxacillin Normon 1 g , Registration No.: 63,636

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Cloxacillin Normon 500 mg

Date of first authorization: January 31, 2001.

Date of last revalidation: October 2010.

Cloxacillin Normon 1 g

Date of first authorization: January 31, 2001.

Date of last revalidation: October 2010.

10. DATE OF TEXT REVIEW

February 2024