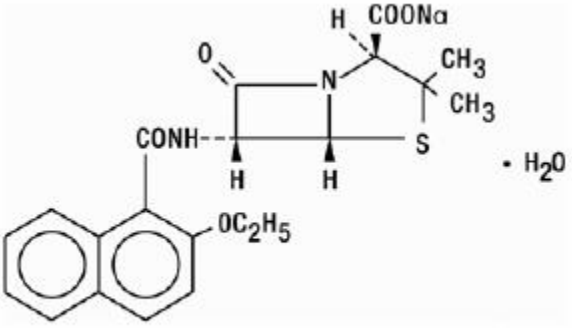
NAFCILLIN - nafcillin sodium injection, powder, for solution
AuroMedics Pharma LLC

PHARMACY BULK PACKAGE - NOT FOR DIRECT INFUSION
To reduce the development of drug-resistant bacteria and maintain the effectiveness of nafcillin for injection and other antibacterial drugs, nafcillin for injection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

DESCRIPTION
Nafcillin for injection, USP is a semisynthetic penicillin derived from the penicillin nucleus, 6-aminopenicillanic acid. The chemical name of nafcillin sodium is Monosodium (2*S*,5*R*,6*R*)-6-(2-ethoxy-1-naphthamido)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylate monohydrate. It is resistant to inactivation by the enzyme penicillinase (beta-lactamase). The structural formula of nafcillin sodium is as follows:



$C_{21}H_{21}N_2NaO_5S{\bullet}H_2O$ M.W. 454.47

Nafcillin for injection, USP for the intravenous route of administration, contains nafcillin sodium as a sterile white to yellowish-white powder for reconstitution. The pH of the reconstituted solution is 6.0 to 8.5. Nafcillin for injection, USP contains nafcillin sodium as the monohydrate equivalent to 10 grams of nafcillin per Pharmacy Bulk Package and is buffered with 40 mg sodium citrate per gram. The sodium content is 65.78 mg [2.9 mEq] per gram.

A Pharmacy Bulk Package is a container of sterile dosage form which contains many single doses. The contents are intended for use in a pharmacy admixture program and are restricted to the preparation of admixtures for intravenous infusion. FURTHER DILUTION IS REQUIRED AFTER RECONSTITUTION (see **DOSAGE AND ADMINISTRATION**, and **DIRECTIONS FOR PROPER USE OF PHARMACY BULK PACKAGE**).

CLINICAL PHARMACOLOGY
In a study of five healthy adults administered a single 500 mg dose of nafcillin by intravenous injection over seven minutes, the mean plasma concentration of the drug was approximately 30 mcg/mL at 5 minutes after injection. The mean area under the plasma concentration-versus-time curve (AUC) for nafcillin in this study was 18.06 mcg•h/mL.

The serum half-life of nafcillin administered by the intravenous route ranged from 33 to 61 minutes as measured in three separate studies.

In contrast to the other penicillinase-resistant penicillins, only about 30% of nafcillin is excreted as unchanged drug in the urine of normal volunteers, and most within the first six hours. Nafcillin is primarily eliminated by nonrenal routes, namely hepatic inactivation and excretion in the bile.

Nafcillin binds to serum proteins, mainly albumin. The degree of protein binding reported for nafcillin is 89.9 ± 1.5%. Reported values vary with the method of study and the investigator.

The concurrent administration of probenecid with nafcillin increases and prolongs plasma concentrations of nafcillin. Probenecid significantly reduces the total body clearance of nafcillin with renal clearance being decreased to a greater extent than nonrenal clearance.

The penicillinase-resistant penicillins are widely distributed in various body fluids, including bile, pleural, amniotic and synovial fluids. With normal doses insignificant concentrations are found in the aqueous humor of the eye. High nafcillin CSF levels have been obtained in the presence of inflamed meninges.

Renal failure does not appreciably affect the serum half-life of nafcillin; therefore, no modification of the usual nafcillin dosage is necessary in renal failure with or without hemodialysis. Hemodialysis does not accelerate the rate of clearance of nafcillin from the blood.

A study which assessed the effects of cirrhosis and extrahepatic biliary obstruction in man demonstrated that the plasma clearance of nafcillin was significantly decreased in patients with hepatic dysfunction. In these patients with cirrhosis and extrahepatic obstruction, nafcillin excretion in the urine was significantly increased from about 30 to 50% of the administered dose, suggesting that renal disease superimposed on hepatic disease could further decrease nafcillin clearance.

Microbiology

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. The drugs in this class are highly resistant to inactivation by staphylococcal penicillinase and are active against penicillinase producing strains of *Staphylococcus aureus*. The penicillinase-resistant penicillins are active *in vitro* against a variety of other bacteria.

Susceptibility Test Methods

When available, the clinical microbiology laboratory should provide the results of *in vitro* susceptibility test results for antimicrobial drugs used in local hospitals and practice areas to the physician as periodic reports that describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting the most effective antimicrobial.

Dilution Techniques

Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized procedure based on dilution method[1,2] (broth, agar or microdilution) or equivalent. It has been reported that determination of susceptibility or resistance of a microorganism to all penicillinase-resistant penicillins, including nafcillin, may be deduced by testing microorganisms against either oxacillin or cefoxitin.[2] For this reason, routine dilution testing of nafcillin is not advised and susceptibility to nafcillin should be determined by dilution using standardized inoculum and concentrations of oxacillin according to the criteria in table 1.[1,2]

Table 1: Staphylococcus aureus MIC Susceptibility Test Interpretive Criteria for Oxacillin[a]

	Minimum Inhibitory Oxacillin Concentrations (mcg/mL)	
Pathogen	**Susceptible (S)**	**Resistant (R)**
Staphylococcus aureus	≤ 2	≥ 4

[a]*Staphylococcus aureus* strains found to be “Susceptible” or “Resistant” to oxacillin by dilution testing can be considered to be “Susceptible” or “Resistant” to nafcillin.

Diffusion Techniques

Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure[2,3] requires the use of standardized inoculum concentrations. It has been reported that determination of susceptibility or resistance of a microorganism to all penicillinase-resistant penicillins, including nafcillin, may be deduced by testing microorganisms against either oxacillin or cefoxitin.[2] Disk diffusion results using cefoxitin have been shown to be more reproducible than those obtained with oxacillin,[4,5] therefore cefoxitin is the preferred reagent for testing nafcillin susceptibility by diffusion. Reports from the laboratory providing results of the standard single-disk susceptibility test with a 30 microgram cefoxitin disk should be interpreted according to the following criteria in Table 2.

Table 2: Staphylococcus aureus Disk Diffusion Susceptibility Test Interpretive Criteria for Nafcillin Using a 30 mcg Cefoxitin Disk[a]

	Disk Diffusion Diameters (mm)	
Pathogen	**Susceptible (S)**	**Resistant (R)**
Staphylococcus aureus	≥ 22	≤ 21

[a]*Staphylococcus aureus* strains found to be “Susceptible” or “Resistant” to cefoxitin by disk diffusion can be considered to be “Susceptible” or “Resistant” to nafcillin.

A report of “Susceptible” indicates that the pathogen is likely to be inhibited by usually achievable concentrations of the antimicrobial compound in blood. A report of “Resistant” indicates that usually achievable concentrations of the antimicrobial compound in the blood are unlikely to be inhibitory and that other therapy should be selected.
Measurement of MIC or MBC and achieved antimicrobial compound concentrations may be appropriate to guide therapy in some infections. (See **CLINICAL PHARMACOLOGY** section for further information on drug concentrations achieved in infected body sites and other pharmacokinetic properties of this antimicrobial drug product.)
Quality Control

Standardized susceptibility test procedures require the use of laboratory control microorganisms to monitor and ensure the accuracy and precision of the supplies and reagents used in the assay, and the techniques of the individuals performing the test. Appropriate quality control organisms and acceptable corresponding ranges of oxacillin MICs obtained by dilution testing or inhibition zones around 30 mcg cefoxitin disks are provided in Table 3.
Table 3: In Vitro Susceptibility Test Quality Control Ranges for Oxacillin and Cefoxitin

Organism (ATCC #)	**Oxacillin MIC range (mcg/mL)**	**Cefoxitin disk diffusion range (mm)**
Staphylococcus aureus (29213)	0.12 - 0.5	Not applicable
Staphylococcus aureus (25923)	Not applicable	23 - 29

INDICATIONS AND USAGE
Nafcillin for injection, USP is indicated in the treatment of infections caused by penicillinase-producing staphylococci which have demonstrated susceptibility to the drug. Culture and susceptibility tests should be performed initially to determine the causative organism and its susceptibility to the drug (see **CLINICAL PHARMACOLOGY - Susceptibility Test Methods**).

Nafcillin for injection, USP may be used to initiate therapy in suspected cases of resistant staphylococcal infections prior to the availability of susceptibility test results. Nafcillin for injection, USP should not be used in infections caused by organisms susceptible to penicillin G. If the susceptibility tests indicate that the infection is due to an organism other than a resistant *Staphylococcus*, therapy should not be continued with nafcillin for injection, USP.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of nafcillin for injection, USP and other antibacterial drugs, nafcillin for injection, USP should be used only to treat or prevent 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.

CONTRAINDICATIONS
A history of a hypersensitivity (anaphylactic) reaction to any penicillin is a contraindication.

WARNINGS
Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins. Before initiating therapy with nafcillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens. If an allergic reaction occurs, nafcillin should be discontinued and appropriate therapy instituted. Serious anaphylactic reactions require immediate emergency treatment with epinephrine. Oxygen, intravenous steroids, and airway management, including intubation, should also be administered as indicated.

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including nafcillin for injection, 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 CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD 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.

PRECAUTIONS

General
Nafcillin should generally not be administered to patients with a history of sensitivity to any penicillin.

Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma. Whenever allergic reactions occur, penicillin should be withdrawn unless, in the opinion of the physician, the condition being treated is life-threatening and amenable only to penicillin therapy. The use of antibiotics may result in overgrowth of nonsusceptible organisms. If new infections due to bacteria or fungi occur, the drug should be discontinued and appropriate measures taken.

The liver/biliary tract is the primary route of nafcillin clearance. Caution should be exercised when patients with concomitant hepatic insufficiency and renal dysfunction are treated with nafcillin. Serum levels should be measured and the dosage adjusted appropriately to avoid possible neurotoxic reactions associated with very high concentrations (see **DOSAGE AND ADMINISTRATION**).

Prescribing nafcillin for injection in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Information for Patients
Patients should be counseled that antibacterial drugs including nafcillin for injection should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When nafcillin for injection is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by nafcillin for injection or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Laboratory Tests
Bacteriologic studies to determine the causative organisms and their susceptibility to the penicillinase-resistant penicillins should be performed (see **CLINICAL PHARMACOLOGY: Microbiology**). In the treatment of suspected staphylococcal infections, therapy should be changed to another active agent if culture tests fail to demonstrate the presence of staphylococci.

Periodic assessment of organ system function including renal, hepatic, and hematopoietic should be made during prolonged therapy with nafcillin.

White blood cell and differential cell counts should be obtained prior to initiation of therapy and periodically during therapy with nafcillin.

Periodic urinalysis, blood urea nitrogen, and creatinine determinations should be performed during therapy with the nafcillin and dosage alterations should be considered if these values become elevated. If any impairment of renal function is suspected or known to exist, a reduction in the total dosage should be considered and blood levels monitored to avoid possible neurotoxin reactions (See **DOSAGE AND ADMINISTRATION**).

SGOT and SGPT values should be obtained periodically during therapy to monitor for possible liver function abnormalities.

Drug Interactions
Tetracycline, a bacteriostatic antibiotic, may antagonize the bactericidal effect of penicillin and concurrent use of these drugs should be avoided.

Nafcillin in high dosage regimens, i.e., 2 grams every 4 hours, has been reported to decrease the effects of warfarin. When nafcillin and warfarin are used concomitantly, the prothrombin time should be closely monitored and the dose of warfarin adjusted as necessary. This effect may persist for up to 30 days after nafcillin has been discontinued.

Nafcillin when administered concomitantly with cyclosporine has been reported to result in subtherapeutic cyclosporine levels. The nafcillin-cyclosporine interaction was documented in a patient during two separate courses of therapy. When cyclosporine and nafcillin are used concomitantly in organ transplant patients, the cyclosporine levels should be monitored.

Drug/Laboratory Test Interactions
Nafcillin in the urine can cause a false-positive urine reaction for protein when the sulfosalicyclic acid test is used, but not with the dipstick.

Carcinogenesis, Mutagenesis, Impairment of Fertility
No long-term animal studies have been conducted with these drugs. Studies on reproduction (nafcillin) in rats and mice reveal no fetal or maternal abnormalities before conception and continuously through weaning (one generation).

Pregnancy

Teratogenic Effects

Pregnancy Category B
Reproduction studies have been performed in the mouse with oral doses up to 20 times the human dose and orally in the rat at doses up to 40 times the human dose and have revealed no evidence of impaired fertility or harm to the rodent fetus due to nafcillin. There are, however, no adequate or well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, nafcillin should be used during pregnancy only if clearly needed.

Nursing Mothers
Penicillins are excreted in human milk. Caution should be exercised when penicillins are administered to a nursing woman.

Pediatric Use
The liver/biliary tract is the principal route of nafcillin elimination. Because of immature hepatic and renal function in pediatric patients, nafcillin excretion may be impaired, with abnormally high serum levels resulting. Serum levels should be monitored and the dosage adjusted appropriately. There are no approved pediatric patient dosage regimens for intravenous nafcillin. Safety and effectiveness in pediatric patients have not been established.

Geriatric Use
Clinical studies of nafcillin for injection did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Nafcillin for injection contains 65.78 mg (2.9 mEq) of sodium per gram. At the usual recommended doses, patients would receive between 197.34 and 394.68 mg/day (8.58 and 17.16 mEq) of sodium. The geriatric population may respond with a blunted natriuresis to salt loading. This may be clinically important with regard to such diseases as congestive heart failure.

ADVERSE REACTIONS
Body as a Whole

The reported incidence of allergic reactions to penicillins ranges from 0.7 to 10 percent (see **WARNINGS**). Sensitization is usually the result of treatment but some individuals have had immediate reactions to penicillin when first treated. In such cases, it is thought that the patients may have had prior exposure to the drug via trace amounts present in milk or vaccines.

Two types of allergic reactions to penicillin are noted clinically, immediate and delayed.

Immediate reactions usually occur within 20 minutes of administration and range in severity from urticaria and pruritus to angioneurotic edema, laryngospasm, bronchospasm, hypotension, vascular collapse, and death. Such immediate anaphylactic reactions are very rare (see **WARNINGS**) and usually occur after parenteral therapy but have occurred in patients receiving oral therapy. Another type of immediate reaction, an accelerated reaction, may occur between 20 minutes and 48 hours after administration and may include urticaria, pruritus, and fever. Although laryngeal edema, laryngospasm, and hypotension occasionally occur, fatality is uncommon.

Delayed allergic reactions to penicillin therapy usually occur after 48 hours and sometimes as late as 2 to 4 weeks after initiation of therapy. Manifestations of this type of reaction include serum sickness-like symptoms (i.e., fever, malaise, urticaria, myalgia, arthralgia, abdominal pain) and various skin rashes. Nausea, vomiting, diarrhea, stomatitis, black or hairy tongue, and other symptoms of gastrointestinal irritation may occur, especially during oral penicillin therapy.
Local Reactions

Pain, swelling, inflammation, phlebitis, thrombophlebitis, and occasional skin sloughing at the injection site have occurred with intravenous administration of nafcillin (see **DOSAGE AND ADMINISTRATION**). Severe tissue necrosis with sloughing secondary to subcutaneous extravasation of nafcillin has been reported.

Nervous System Reactions

Neurotoxic reactions similar to those observed with penicillin G could occur with large intravenous or intraventricular doses of nafcillin especially in patients with concomitant hepatic insufficiency and renal dysfunction (see **PRECAUTIONS**).

Urogenital Reactions

Renal tubular damage and interstitial nephritis have been associated infrequently with the administration of nafcillin. Manifestations of this reaction may include rash, fever, eosinophilia, hematuria, proteinuria, and renal insufficiency.

Gastrointestinal Reactions

Pseudomembranous colitis has been reported with the use of nafcillin. The onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (see **WARNINGS**).

Metabolic Reactions

Agranulocytosis, neutropenia, and bone marrow depression have been associated with the use of nafcillin.

To report SUSPECTED ADVERSE EVENTS, contact FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE

Neurotoxic reactions similar to those observed with penicillin G may arise with intravenous doses of nafcillin especially in patients with concomitant hepatic insufficiency and renal dysfunction (see **PRECAUTIONS**).

In the case of overdosage, discontinue nafcillin, treat symptomatically and institute supportive measures as required. Hemodialysis does not increase the rate of clearance of nafcillin from the blood.

DOSAGE AND ADMINISTRATION

Nafcillin for injection Pharmacy Bulk Package is available for intravenous use only. The usual I.V. dosage for adults is 500 mg every 4 hours. For severe infections, 1 gram every 4 hours is recommended. Administer slowly over at least 30 to 60 minutes to minimize the risk of vein irritation and extravasation.

Bacteriologic studies to determine the causative organisms and their susceptibility to nafcillin should always be performed. Duration of therapy varies with the type and severity of infection as well as the overall condition of the patient; therefore, it should be determined by the clinical and bacteriological response of the patient. In severe staphylococcal infections, therapy with nafcillin should be continued for at least 14 days. Therapy should be continued for at least 48 hours after the patient has become afebrile, asymptomatic, and cultures are negative. The treatment of endocarditis and osteomyelitis may require a longer duration of therapy.

Concurrent administration of the penicillinase-resistant penicillins and probenecid increases and prolongs serum penicillin levels. Probenecid decreases the apparent volume of distribution and slows the rate of excretion by competitively inhibiting renal tubular secretion of penicillin. Nafcillin-probenecid therapy is generally limited to those infections where very high serum levels of nafcillin are necessary.

No dosage alterations are necessary of patients with renal dysfunction, including those on hemodialysis. Hemodialysis does not accelerate nafcillin clearance from the blood.

For patients with hepatic insufficiency and renal failure, measurement of nafcillin serum levels should be performed and dosage adjusted accordingly.

With intravenous administration, particularly in elderly patients, care should be taken because of the possibility of thrombophlebitis.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

Do not add supplementary medication to nafcillin.

Oral preparation of the penicillinase-resistant penicillins should not be used as initial therapy in serious life-threatening infections (see **PRECAUTIONS, General**). Oral therapy with the penicillinase-resistant penicillins may be used to follow-up the previous use of a parenteral agent as soon as the clinical condition warrants. With intravenous administration, particularly in elderly patients, care should be taken because of the possibility of thrombophlebitis.

DIRECTIONS FOR PROPER USE OF A PHARMACY BULK PACKAGE

The container closure may be penetrated only one time after reconstitution using a suitable sterile transfer device or dispensing set which allows measured dispensing of the contents. Use of a syringe and needle is not recommended as it may cause leakage. Use of this product is restricted to a suitable work area, such as a laminar flow hood. The withdrawal of container contents should be accomplished without delay. However, should this not be possible, a maximum of **4 HOURS** from initial closure entry is permitted to complete fluid transfer operations. This time limit should begin with the introduction of solvent or diluent into the Pharmacy Bulk Package bottle.

Pharmacy Bulk Package

Each nafcillin for injection, USP Pharmacy Bulk Package bottle contains nafcillin sodium as the monohydrate equivalent to 10 g nafcillin. The Pharmacy Bulk Package bottle is intended for use in a pharmacy admixture program and is restricted to the preparation of admixtures for intravenous infusion. Add 93 mL Sterile Water for Injection, USP or 0.9% Sodium Chloride Injection, USP. The resulting solution will contain 100 mg nafcillin activity per mL and will require further dilution.

CAUTION: NOT TO BE DISPENSED AS A UNIT.

Do not add supplementary medication to nafcillin.

DIRECTIONS FOR USE

For Administration by Intravenous Drip: Reconstitute as directed above (For Intravenous Use) prior to diluting with intravenous solution.

STABILITY PERIODS FOR NAFCILLIN FOR INJECTION, USP*

Concentration mg/mL	**Sterile Water for Injection USP**	**Sodium Chloride Injection USP (0.9%)**	**Sodium Lactate Solution USP (M/6 Molar)**	**Dextrose Injection USP (5%)**	**Dextrose and Sodium Chloride Injection USP (5% Dextrose and 0.45% Sodium Chloride)**	**Invert Sugar Injection USP (10%)**	**Lactated Ringer's Injection USP**
ROOM TEMPERATURE (25ºC)							
10-200	24 Hrs	24 Hrs					
30			24 Hrs				
2-30				24 Hrs	24 Hrs		
10-30						24 Hrs	24 Hrs
REFRIGERATION (4ºC)							
10-200	7 Days	7 Days					
10-30			7 Days	7 Days	7 Days	7 Days	7 Days
FROZEN (-15ºC)							
250	90 Days	90 Days					
10-250			90 Days	90 Days	90 Days	90 Days	90 Days

* IMPORTANT: This chemical stability information in no way indicates that it would be acceptable practice to use this product well after the preparation time. Good professional practice suggests that a product should be used as soon after preparation as feasible.

Only those solutions listed above should be used for the intravenous infusion of nafcillin sodium. The concentration of the antibiotic should fall within the range specified. The drug concentration and the rate and volume of the infusion should be adjusted so that the total dose of nafcillin is administered before the drug loses its stability in the solution in use.

There is no clinical experience available on the use of this agent in neonates or infants for this route of administration.

This route of administration should be used for relatively short-term therapy (24 to 48 hours) because of the occasional occurrence of thrombophlebitis particularly in elderly patients.

If another agent is used in conjunction with nafcillin therapy, **it should not be physically mixed** with nafcillin but should be administered separately.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

HOW SUPPLIED

Each nafcillin for injection, USP Pharmacy Bulk Package bottle contains nafcillin sodium equivalent to 10 grams of nafcillin.

Nafcillin for Injection, USP is a sterile, white to yellowish-white powder supplied in Pharmacy Bulk Package bottles as follows:

Nafcillin for Injection USP, 10 g
Pharmacy Bulk Package bottles in a Box of 1 NDC 55150-124-99

Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

The container closure is not made with natural rubber latex.

REFERENCES

1. Clinical and Laboratory Standards Institute. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard-Eighth Edition.* CLSI Document M07-A8 (ISBN 1-56238-689-1). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2009.

2. Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing; Twenty-First Informational Supplement.* CLSI Document M100S21 (ISBN 1-56238-742-1). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2011.

3. Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard-Tenth Edition.* CLSI Document M02-A10 (ISBN 1-56238-688-3). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2009.

4. Palazzo ICV, Darini ALC. Evaluation of methods for detecting oxacillin resistance in coagulase-negative staphylococci including cefoxitin disc diffusion. FEMS Microbiol Lett 2006;257:299-305.

5. Swenson JM, Tenover FC; Cefoxitin Disk Study Group. Results of disk diffusion testing with cefoxitin correlate with presence of mecA in *Staphylococcus* spp. J Clin Microbiol 2005;43:3818-23.

Manufactured for:
AuroMedics Pharma LLC
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Dayton, NJ 08810

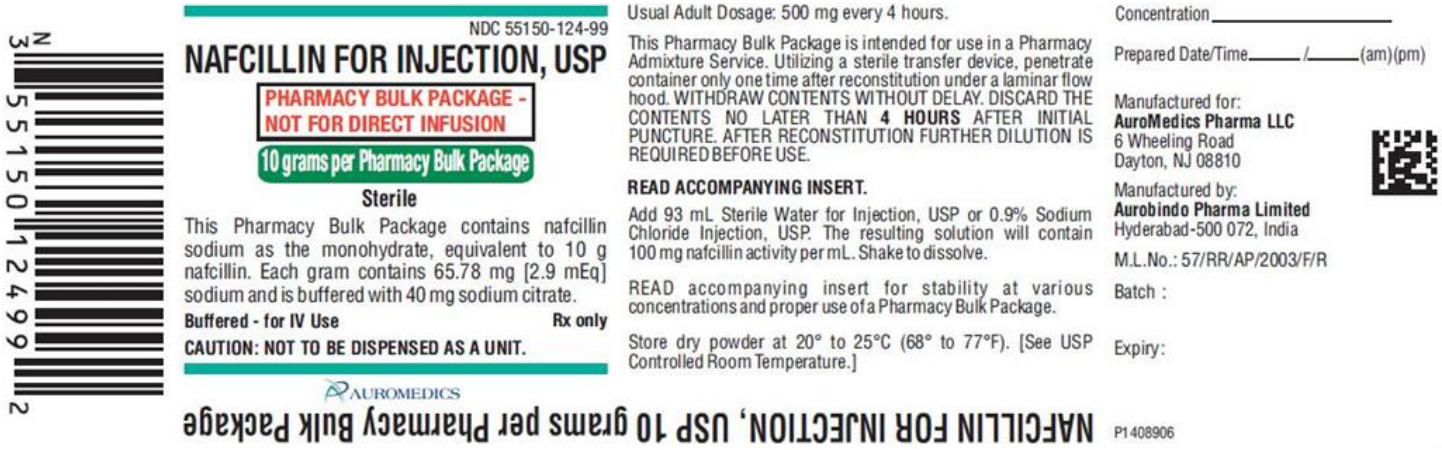
Manufactured by:
Aurobindo Pharma Limited
Hyderabad-500 072, India

Issued: December 2011

PACKAGE LABEL-PRINCIPAL DISPLAY PANEL - 10 G PHARMACY BULK PACKAGE LABEL
NDC 55150-124-99
NAFCILLIN FOR INJECTION, USP
PHARMACY BULK PACKAGE -
NOT FOR DIRECT INFUSION
10 grams per Pharmacy Bulk Package
Sterile

This Pharmacy Bulk Package contains nafcillin sodium as the monohydrate, equivalent to 10 g nafcillin. Each gram contains 65.78 mg [2.9 mEq] sodium and is buffered with 40 mg sodium citrate.

Buffered - for IV Use **Rx only**
CAUTION: NOT TO BE DISPENSED AS A UNIT.
AUROMEDICS



PACKAGE LABEL-PRINCIPAL DISPLAY PANEL - 10 G PHARMACY BULK PACKAGE BOX LABEL
Rx only **NDC 55150-124-99**
NAFCILLIN FOR INJECTION, USP
PHARMACY BULK PACKAGE -
NOT FOR DIRECT INFUSION
10 grams per Pharmacy
Bulk Package
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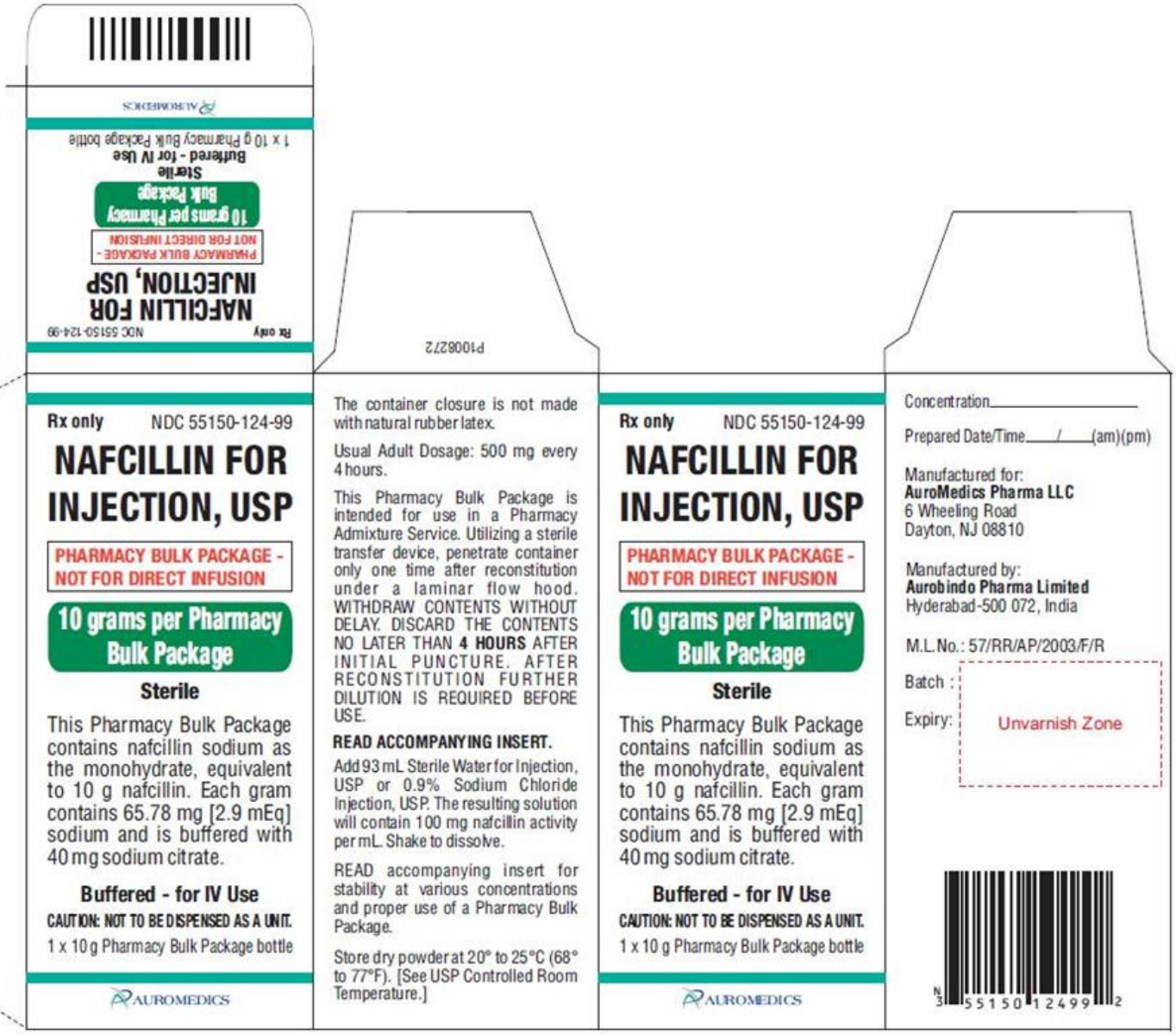
This Pharmacy Bulk Package contains nafcillin sodium as the monohydrate, equivalent to 10 g nafcillin. Each gram contains 65.78 mg [2.9 mEq] sodium and is buffered with 40 mg sodium citrate.
Buffered - for IV Use
CAUTION: NOT TO BE DISPENSED AS A UNIT.
1 x 10 g Pharmacy Bulk Package bottle
AUROMEDICS



Rx only NDC 55150-124-99

NAFCILLIN FOR INJECTION, USP

PHARMACY BULK PACKAGE - NOT FOR DIRECT INFUSION

10 grams per Pharmacy Bulk Package

Sterile

This Pharmacy Bulk Package contains nafcillin sodium as the monohydrate, equivalent to 10 g nafcillin. Each gram contains 65.78 mg [2.9 mEq] sodium and is buffered with 40 mg sodium citrate.

Buffered - for IV Use

CAUTION: NOT TO BE DISPENSED AS A UNIT.

1 x 10 g Pharmacy Bulk Package bottle

AUROMEDICS

The container closure is not made with natural rubber latex.

Usual Adult Dosage: 500 mg every 4 hours.

This Pharmacy Bulk Package is intended for use in a Pharmacy Admixture Service. Utilizing a sterile transfer device, penetrate container only one time after reconstitution under a laminar flow hood. WITHDRAW CONTENTS WITHOUT DELAY. DISCARD THE CONTENTS NO LATER THAN **4 HOURS** AFTER INITIAL PUNCTURE. AFTER RECONSTITUTION FURTHER DILUTION IS REQUIRED BEFORE USE.

READ ACCOMPANYING INSERT.

Add 93 mL Sterile Water for Injection, USP or 0.9% Sodium Chloride Injection, USP. The resulting solution will contain 100 mg nafcillin activity per mL. Shake to dissolve.

READ accompanying insert for stability at various concentrations and proper use of a Pharmacy Bulk Package.

Store dry powder at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]

Rx only NDC 55150-124-99

NAFCILLIN FOR INJECTION, USP

PHARMACY BULK PACKAGE - NOT FOR DIRECT INFUSION

10 grams per Pharmacy Bulk Package

Sterile

Buffered - for IV Use

1 x 10 g Pharmacy Bulk Package bottle

AUROMEDICS

P1008272

Rx only NDC 55150-124-99

NAFCILLIN FOR INJECTION, USP

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10 grams per Pharmacy Bulk Package

Sterile

Buffered - for IV Use

1 x 10 g Pharmacy Bulk Package bottle

AUROMEDICS

Concentration_____

Prepared Date/Time____/____(am)(pm)

Manufactured for:
AuroMedics Pharma LLC
6 Wheeling Road
Dayton, NJ 08810

Manufactured by:
Aurobindo Pharma Limited
Hyderabad-500 072, India

M.L.No.: 57/RR/AP/2003/F/R

Batch :

Expiry:

Unvarnish Zone

N 3 55150 12499 2