To reduce the development of drug-resistant bacteria and maintain the efficacy 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, anti-bacterial penicillin derived from the penicillin nucleus 6-aminopenicillanic acid. It is the sodium salt of a penicillanic acid derivative.

The chemical name is 6-THA-2-carboxylic acid, 6-[(2-ethoxy-1-naphthalenyl)carbonyl]amino]-3,3-dimethyl-7-oxo-monoacid sodium, monohydrate (2/3H2O,5NaO). It is resistant to inactivation by the enzyme penicillinase (beta-lactamase). The structural formula of nafcillin sodium is as follows:

\[
\text{C}_{21}\text{H}_{21}\text{N}_{2}\text{NaO}_{5}\text{S} \cdot \text{H}_{2}\text{O} \cdot 4\text{H}_{2}\text{O} \quad \text{M.W.} 454.47
\]

Each Nafcillin for Injection, USP Pharmacy Bulk Package is supplied as a dry powder in bottles containing nafcillin sodium and is intended for intravenous administration. The pH of the solution ranges from 6.0 to 6.6. Each Pharmacy Bulk Package bottle contains nafcillin sodium, as the monohydrate equivalent to 10 grams of nafcillin. The sodium content is 65 mg per 5 mL (2.9 mL) per gram of nafcillin. The product is buffered with 45 mg sodium citrate per gram.

Nafcillin is indicated in the treatment of infections caused by penicillinase-producing bacteria, and it is particularly suitable for infections caused by penicillin-resistant strains of the following microorganisms, in vitro:

- Staphylococcus aureus (including strains which are known or are strongly suspected to be caused by bacteria.

- Staphylococcus pyogenes (including penicillinase-producing strains).

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 bacteria.

CONTRAINDICATIONS:
- 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 receiving penicillin derivatives. Therefore, prior to the administration of Nafcillin for Injection, all patients, with or without a history of penicillin allergies, should be questioned concerning previous sensitivity.

- The possibility of a patient’s being more susceptible to a methicillin-resistant Staphylococcus spp. than to a methicillin-sensitive Staphylococcus spp. should be considered.

- If only one or a few recent infections due to bacteria or fungi occur, the drug should be discontinued and appropriate measures taken.

- If new infections due to bacteria or fungi occur, the drug should be discontinued and appropriate measures taken.

- Nafcillin when administered concomitantly with cyclosporine has been reported to cause increased serum cyclosporine levels for up to 30 days after nafcillin has been discontinued.

- When cyclosporine and nafcillin are used concomitantly, the 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.

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

- Nafcillin binds to serum proteins, mainly albumin. The degree of binding is related to the concentration of nafcillin. In clinical studies, nafcillin protein binding ranged from 89 to 91%. Reduced values vary with the method of isolation of the drug.

- The concurrent administration of probenecid with nafcillin increases and prolongs plasma concentrations of nafcillin. Probenecid is known to reduce renal clearance by decreasing the rate of glomerular filtration and reabsorption in the tubules. Probenecid binds to serum proteins, mainly albumin. The degree of binding is related to the concentration of nafcillin. In clinical studies, nafcillin protein binding has ranged from 89 to 91.

- A study which assessed the effects of erections and catharsis in patients given Nafcillin for Injection should be discontinued and alternate therapy provided. Nafcillin should be used with caution in individuals with histories of significant diuresis and the patient should be monitored closely for hyperpyrexia and other signs of fluid and electrolyte abnormalities.

- Excessive oral administration of Nafcillin for Injection may range in severity from mild diarrhea to fatal colitis. Treatment with Nafcillin for Injection should be discontinued and appropriate measures taken.

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- In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

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of subjects aged 65 and over to determine whether they respond differently than younger subjects. Other reported clinical experiences have not iden-
tified differences in responses between the elderly and younger patients. In general, geriatric patients should usually be started at the starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, and cardiac function, and of concomitant dis-
cease or other drug therapy.
Each Pharmacy Bulk Package bottle contains nafcillin sodium, as the monohydrate equivalent to 10 grams of nafcillin. The sodium content is 65.8 mg [2.9 mEq] per gram of nafcillin. The product is buffered with 40 mg sodium citrate per gram. At the usual recommended doses, patients reach an intravascular concentration varying from 10 to 250 mg/mL. With intravenous doses of nafcillin, especially in patients with concomitant hepatic insufficiency and renal dysfunction, the peak serum concentration may occur with large intravenous or intraventricular doses of nafcillin especially in patients with concomitant hepatic insufficiency and renal dysfunction.
Gastrointestinal Reactions
Intestinal irritation may occur, especially during oral penicillin therapy. Administration of nafcillin (see PRECAUTIONS) may be physically mixed in patients with concomitant hepatic insufficiency and renal dysfunction.

Metabolic Reactions
Anaphylaxis, anaphylactoid reactions, and skin reactions have occurred, fatality is uncommon. Delayed allergic reactions to penicillin ther-
apy 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 reactions (i.e., fever, rash, urticaria, musculoskeletal, arthropathy, abdominal pain) and various skin rashes. Nausea, vomiting, diarrhea, stomatitis, black or hairy tongue, and other symptoms of gas-
throsis usually occur after 48 hours and sometimes 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.

ADVERSE REACTIONS:
Body as a Whole
The incidence of adverse reactions to penicillins ranges from 0.7 to 10 percent (see WARNINGS). For the most part, these reactions have been mild and non-life-threatening. The most common reactions occur after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Immediate reactions usually occur within 30 minutes of administration and range in severity from urticaria and pruritus to angioedema, laryngospasm, bronchospasm, hypotension, vascular collapse, and death. Such immediate anaphylactic reactions are very rare (see WARNINGS).

Nafcillin for Injection should be used in conjunction with other antibacterial drugs in the future. The resulting solution will contain 100 mg nafcillin per mL and will require further dilution.

CAUTION: NOT TO BE DISPENSED AS A UNIT
DIRECTIONS FOR USE
Concentrate as directed above (For Intravenous Use) prior to diluting with intravenous solution.

STABILITY PERIODS FOR NAFCILLIN FOR INJECTION, USP*

ROOM TEMPERATURE (25°C)

athon 12 24 48 hrs
30 days 30 days 30 days
60 days 60 days 60 days
90 days 90 days 90 days

Freeze
12 24 48 hrs
30 days 30 days 30 days
60 days 60 days 60 days
90 days 90 days 90 days

Stability Periods: The period of stability given above is for intact containers and as long as the container is not opened. Any container opened and not stored properly as described above should not be used.

DIRECTIONS FOR PROPER USE OF PHARMACY BULK PACKAGE:
Do not add supplementary medication to Nafcillin for Injection, USP.

DIRECTIONS FOR PROPER USE OF PHARMACY BULK PACKAGE:

DOSAGE AND ADMINISTRATION:
Nafcillin for Injection, in the Pharmacy Bulk Package Bottle is for intra-
vavenous injection only.

The usual IV dosage for adults is 500 mg every 4 hours. For severe infec-
tions, 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.

Overdosage:

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.

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Bacteriologic studies to determine the causative organisms and their sus-
cceptibility to nafcillin should always be performed. Duration of therapy
varies with the type and severity of infection as well as the overall condi-
tion of the patient. Generally, in patients with uncomplicated infections the bacteriologic response of the patient. In severe staphylococcal infec-
tions, therapy with nafcillin should be continued for at least 4 days. The thorough investigation and consultation of the physician are required.

No dosage adjustments are necessary for patients with renal dysfunction, including those on hemodialysis. Hemodialysis does not accelerate nat-
cillin clearance from the blood.

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 mat-
ter and discoloration prior to administration whenever solution and con-
tainer permit.

Do not add supplementary medication to Nafcillin for Injection, USP.

DIRECTIONS FOR PROPER USE OF PHARMACY BULK PACKAGE:

DOSAGE AND ADMINISTRATION:

Nafcillin for Injection may be used only once time after prepara-
tion, utilizing a suitable sterile dispensing set which allows measurement of the solution of nafcillin for injection and of subsequent dis-
case or other drug therapy.

Each PharmacyBulk Package bottle contains nafcillin sodium as the monohydrate equivalent to 10 grams nafcillin and is supplied as for use in the pharmacy in preparing IV additives. Add 90 mL Sterile Water for Injection, USP or 0.9% Sodium Chloride Injection, USP. The resulting solution will contain 100 mg nafcillin per mL and will require further dilution.