When available, the clinical microbiology laboratory should provide the results of Susceptibility Test Methods, indicating that the pathogen is likely to be inhibited by nafcillin in high dosage regimens. A report of “Susceptible” indicates that usually achievable concentrations of this antibiotic in serum and other tissues will inhibit the growth of the test pathogen when the antibiotic is administered with other suitable agents. However, physical and chemical conditions that may affect antibiotic activity may signify that susceptibility information is not applicable to the pathogen being tested or to the method used for susceptibility testing. Resistant strains may require alternative antibiotic therapy. All penicillinase-resistant penicillins should be used only to treat infections that are proven or strongly suspected to be caused by susceptible pathogens.

CLINICAL PHARMACOLOGY:
In clinical studies, nafcillin 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, 5 minutes after injection. The mean area under the plasma concentration-versus-time curve (AUC) for nafcillin in this study was 10 mcg.min/mg/kg, in contrast to the other penicillinase-resistant penicillins, only about 30% of nafcillin is excreted unchanged in the urine and a variable amount of nafcillin, and less so cephalothin and ceftazidime, is excreted biologically active by renal mechanisms, namely, renal tubular reabsorption and excretion in the bile. The importance of renal elimination of nafcillin is reflected by the finding that the renal clearance of nafcillin (ClR) in humans is equal to one and a half times the total body clearance of nafcillin with renal clearance being decreased to a greater degree than the total body clearance. The penicillinase-resistant penicillins are widely distributed in various body fluids, including bile, sputum, and amniotic fluid. With normal dose, insignificant concentrations are found in the aqueous humor of the eye. High nafcillin CSF levels have been reported in cases of meningitis and encephalitis. Renal failure does not affect the apparent half-life of nafcillin; therefore, no modification of the usual dosage of nafcillin is necessary in renal failure with or without hemodialysis. Hemodialysis does not accelerate the rate of clearance of nafcillin from the plasma.

A study which assessed the effects of cirrhosis and enteral bacterial overgrowth on renal clearance demonstrated that the plasma clearance of nafcillin was decreased to the extent that its total body clearance of nafcillin with renal clearance being decreased to a greater degree than the total body clearance. The penicillinase-resistant penicillins are widely distributed in various body fluids, including bile, sputum, and amniotic fluid. With normal dose, insignificant concentrations are found in the aqueous humor of the eye. High nafcillin CSF levels have been reported in cases of meningitis and encephalitis. Renal failure does not affect the apparent half-life of nafcillin; therefore, no modification of the usual dosage of nafcillin is necessary in renal failure with or without hemodialysis. Hemodialysis does not accelerate the rate of clearance of nafcillin from the plasma.

The penicillinase-resistant penicillins are widely distributed in various body fluids, including bile, sputum, and amniotic fluid. With normal dose, insignificant concentrations are found in the aqueous humor of the eye. High nafcillin CSF levels have been reported in cases of meningitis and encephalitis. Renal failure does not affect the apparent half-life of nafcillin; therefore, no modification of the usual dosage of nafcillin is necessary in renal failure with or without hemodialysis. Hemodialysis does not accelerate the rate of clearance of nafcillin from the plasma.

A study which assessed the effects of cirrhosis and enteral bacterial overgrowth on renal clearance demonstrated that the plasma clearance of nafcillin was decreased to the extent that its total body clearance of nafcillin with renal clearance being decreased to a greater degree than the total body clearance. The penicillinase-resistant penicillins are widely distributed in various body fluids, including bile, sputum, and amniotic fluid. With normal dose, insignificant concentrations are found in the aqueous humor of the eye. High nafcillin CSF levels have been reported in cases of meningitis and encephalitis. Renal failure does not affect the apparent half-life of nafcillin; therefore, no modification of the usual dosage of nafcillin is necessary in renal failure with or without hemodialysis. Hemodialysis does not accelerate the rate of clearance of nafcillin from the plasma.

The penicillinase-resistant penicillins are widely distributed in various body fluids, including bile, sputum, and amniotic fluid. With normal dose, insignificant concentrations are found in the aqueous humor of the eye. High nafcillin CSF levels have been reported in cases of meningitis and encephalitis. Renal failure does not affect the apparent half-life of nafcillin; therefore, no modification of the usual dosage of nafcillin is necessary in renal failure with or without hemodialysis. Hemodialysis does not accelerate the rate of clearance of nafcillin from the plasma.
Nafcillin when administered concomitantly with cyclosporins has been reported to result in increased renal insufficiency. The cause of this interaction is unknown. The cyclosporin interaction was documented in a patient during two separate courses of nafcillin given concomitantly in organ transplant patients, the cyclosporine levels should be monitored.

Drug/Laboratory Test Interactions
Nafcillin has been shown to produce a positive urine reaction for protein when the sulfosalicylic acid test is used but is not diabetogenic.

Contraindications
No long-term animal studies have been conducted with these drugs. Skin test reactivity to nafcillin in rats and mice may reveal no material abnormalities before conception and continuously through weaning (see genotoxicity).

Pregnancy: Teratogenic Effects
Precaution Category B
Nafcillin has been shown in animal studies to be diabetogenic.

Nursing Mothers
Porcine nafcillin is used in human milk. Caution should be exercised when porcine antibiotics are administered to a nursing woman.

Pediatric Use
The nafcillin plasma level is the principal route of nafcillin elimination. Because of immature hepatic and renal function in pediatric patients, nafcillin excretion may be delayed, especially in patients with renal impairment. Administration dosage should be monitored and the dosage adjusted appropriately. There are no appropriate animal studies from which to estimate the response of the nursing foetus. 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 response to the elderly and younger patients. In general, dose selection for an elderly patient should be based on the same drug-related principles that guide selection of the dosage for other patients and should be reflected in the administration dosage (see DOSAGE AND ADMINISTRATION).

Adverse Reactions
The reported incidence of allergic reactions to penicillin ranges from 0.7 to 10 per 1,000 patients treated.' The most common manifestations are rash, fever, eosinophilia, hematuria, proteinuria, and renal insufficiency. Frequently with the administration of nafcillin. Manifestations of this reaction may occur between 131.6 and 394.8 mg/day (5.8 and 17.4 mEq) of sodium. The geriatric population may require a sodium reduction to control weight gain and/or a renal insufficiency reaction due to sodium loading.

Dosage Administration
Nafcillin for Injection is available for intramuscular and intravenous use. The resulting solution should be administered by deep intramuscular injection. The recommended dosage of nafcillin for treatment of infection caused by Staphylococcus aureus is 10 to 30 mg/kg every 4 hours. The duration of therapy may vary and should be based on the clinical response of the patient.

Dosage Administration
Nafcillin for Injection contains sodium chloride 15 mEq/mL. The presence of sodium chloride in the endotoxin-coated filter provides an additional means of measuring mean systemic resistance during endotoxin challenge. Nafcillin is contraindicated in patients with a history of anaphylaxis or a systemic anaphylactic reaction to penicillins. Nafcillin is not recommended for use in patients with a known hypersensitivity to penicillins. Nafcillin is not recommended for use in patients with a history of immediate or delayed hypersensitivity reactions to penicillins.

Stability Periods for Nafcillin for Injection, USP*

REFERENCES: