DISCLAIMER

All labeling reflected on this website is for informational and promotional purposes only. It is not intended to be used by healthcare professionals or patients for the purpose of prescribing or administering these products. Questions regarding the current content of product labeling should be directed to Akorn's Customer Service department at 800.932.5676.
Capastat Sulfate is a polypeptide antibiotic isolated from Streptomyces caprae. It is a complex of 4 microbiologically active components which have been characterized in part; however, complete structural determination of all the components has not been established.

Capreomycin is supplied as the dihydrate salt and is soluble in water. In complete solution, it is almost colorless. Each vial contains the equivalent of 1 g capreomycin activity.

The structural formula is as follows:

**INDICATIONS AND USES**

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**CLINICAL PHARMACOLOGY**

Capreomycin is not absorbed in significant quantities from the gastrointestinal tract and must be administered parenterally. In 2 and 3 healthy volunteers, peak capreomycin concentrations in plasma after intramuscular administration of 1 g were reached in 2 hours after administration, and average peak levels reached were 28 and 32 mg/L, respectively (range, 20 to 47 mg/L). Low serum concentrations are present in the serum for at least 30 days after intramuscular administration. The half-life of capreomycin accumulation in subjects with normal renal function. Two patients with marked reduction of renal function had high serum concentrations 24 hours after administration of the drug. When a 1-g dose of capreomycin was given intramuscularly to normal volunteers, 52% was excreted in the urine within 12 hours.

Lehmann, et al., examined the pharmacokinetics of single dose capreomycin (1.5 g) administered intramuscularly and by intravenous infusion. In both healthy volunteers, and under the serum concentration versus time curve was similar for the two routes of administration. Capreomycin peak concentrations after intravenous infusion were 30 ± 47% higher than after intramuscular administration.

Paper chromatographic studies indicated that capreomycin is excreted essentially unaltered. Urine concentrations averaged 1.86 ± 0.67 mg/mL; in 24 hours, volume 275 ± 50 mL. Half-life was 3.1 hours following a 1-g dose.

**Microbiology**

Capreomycin is active against strains of Mycobacterium tuberculosis found in humans. Susceptibility Tests

The minimum inhibitory concentrations of strains of M. tuberculosis to capreomycin vary with the media and techniques employed. In general, the minimum inhibitory concentrations for M. tuberculosis are found in liquid media that are free of egg protein (Thiotub or Dubos) and range from 1 to 5 μg/mL. When the indirect method is used, comparable inhibitory concentrations are obtained when Thiotub agar is used for direct susceptibility testing. When indirect susceptibility tests are performed on standard tuba slants with Thiotub media, susceptibles show rise up to 10 mg/mL and isoniazid, 750 mg/mL. Quantiomyin-containing media, such as Ljoderei-Jensen or ATS, require concentrations of 25 to 50 mg/mL to inhibit susceptible strains. Cross-Resistance

Frequent cross-resistance occurs between capreomycin and viomycin. Varying degrees of cross-resistance between capreomycin and kanamycin and neomycin have been reported. No cross-resistance has been observed between capreomycin and isoniazid, amikacin, or streptomycin. Interstrain methylin salicylic acid, and streptomycin) have been ineffective or cannot be used because of toxicity or the presence of resistant strains of M. tuberculosis found in humans.

Suscetibility studies should be performed to determine the presence of a capreomycin-susceptible strain of M. tuberculosis.

**CONTRAINICATION**

Capastat Sulfate is contraindicated in patients who are hypersensitive to capreomycin.

**PRECAUTIONS**

General

Automated measurements and assessment of well-being function should be performed prior to initiation of therapy with Capastat Sulfate on a regular basis during treatment. Renal injury, with tubular necrosis, elevation of the blood urea nitrogen (BUN) or serum creatinine, and abnormal urinary sediment, has been reported in patients with normal renal function. The clinical significance of the abnormal urinary sediment and slight elevation in the BUN (or serum creatinine) observed during long-term therapy with Capastat Sulfate has not been established.

The peripheral neurovascular blockading action that has been attributed to other polypeptide antibiotics (cortisone, salicylic acid, amikacin, and streptomycin) has not been found or observed in the serum of patients treated with capreomycin. The clinical significance of abnormal urinary sediment and slight elevation in the BUN (or serum creatinine) observed during long-term therapy with Capastat Sulfate has not been established.

Drug Interactions

For conduction of the blocking action of this drug, see PRECAUTIONS. General

Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies have not been performed to determine the effect of capreomycin on clastogenicity, mutagenicity, or impairment of fertility.

Usage in Pregnancy — Pregnancy Category C

Capastat Sulfate has been shown to be teratogenic in rats when given in doses 3.5 to 3 times the human dose. There are no adequate and well-controlled studies in pregnant women. Capastat Sulfate should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus (see PRECAUTIONS, ANIMAL PHARMACOLOGY).

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Capastat Sulfate is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

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Geriatric Use

Clinical studies of Capastat Sulfate did not analyze the safety and efficacy of patients aged 65 and over to determine whether they respond differently from younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, a lower initial selection for an elderly patient should be cautious, usually starting at the low end of the dosage range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant diseases or other drug therapy.

Capastat Sulfate is known to be substantially excreted by the kidney (see CLINICAL PHARMACOLOGY), and the risk of toxic reactions may be greater in patients with impaired renal function. Elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see PRECAUTIONS, ANIMAL PHARMACOLOGY).

Pediatric Usage: NOT FOR PEDIATRIC USE

**WARNINGS**

The use of Capastat Sulfate (Capreomycin for Injection, USP) in patients with renal insufficiency or preexisting auditory impairment must be undertaken with great caution. In the rare case of additional renal nerve VIII impairment or renal injury also be weighed against the benefits to be derived from therapy.

Roter AMMANN, ANIMAL PHARMACOLOGY, and ANIMAL TOXICITY INFORMATION.

Since other parenteral antituberculosis agents (streptomycin, isoniazid, amikacin, gentamicin, tobramycin, kanamycin, and neomycin) have been reported. No cross-resistance has been observed between capreomycin and isoniazid, amikacin, or streptomycin. Interstrain methylin salicylic acid, and streptomycin) have been ineffective or cannot be used because of toxicity or the presence of resistant strains of M. tuberculosis found in humans.

Suscetibility studies should be performed to determine the presence of a capreomycin-susceptible strain of M. tuberculosis. Caution should be exercised in the administration of antibiotics, including Capastat Sulfate, to any patient who has demonstrated some form of allergy, particularly to drugs.

Laboratory Tests

Tests of renal function should be made throughout the period of treatment, and reduced dosage should be employed in patients with known or suspected renal impairment.

Renal function studies should be made both before therapy with Capastat Sulfate is started and on a weekly basis during treatment. Since hyaluronidase, hyaluronidase and hyaluronidase may occur during therapy, these serum electrolyte levels should be determined periodically.

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Nephrotoxicity: In 38% of 722 patients treated with Capastat, siloxane of the BLN above 20 m g/kg has been observed. In many instances, there was also depression of PISP excretion and abnormal urine sediment. In 10% of these, the BLN elevation exceeded 30 mg/kg.

Toxic nephritis was reported in 1 patient with tuberculosis and portal cirrhosis who was treated with Capastat Sulfate (1 g) and amoxicillin deoxycholate daily for 1 month. This patient developed insufficiency and oliguria and died. Autopsy showed subsiding subclinical auditory loss noted in approximately 11% of 722 patients undergoing treatment with Capastat Sulfate. This was a 5- to 10-day delay in the 4000- to 8000-CPS range. Clinically apparent hearing loss occurred in 3% of the 722 subjects. Some patients reported changes in taste. Other cases with permanent loss were not progressive following withdrawal of Capastat Sulfate.

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Tinnitus and vertigo have occurred. Abnormal results in liver function tests have occurred in many persons receiving Capastat Sulfate in producing these abnormalities is not clear; however, periodic determinations of liver function are recommended.

Intramuscularly subcutaneous needle may be associated with increased pain and the development of sterile abscesses. Patients who have received an overdose of capreomycin and have normal renal function should be carefully hydrolyzed to maintain a urine output of 3 to 5 ml/kg/h. Fluid balance, electrolytes, and creatinine clearance should be carefully monitored.

Hypersensitivity: Urticaria and maculopapular skin rashes associated in some cases with febrile reactions have been reported. Drug-induced hepatitis and other antituberculosis drugs have been given concomitantly.

Capastat Sulfate Solution may acquire a pale straw color and darken with time, but this is not associated with loss of potency or the development of toxicity. After reconstitution, all solutions of Capastat Sulfate may be stored for up to 24 hours under refrigeration.

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Gastric emptying or charcoal. When Capastat Sulfate and other antituberculosis drugs were given concomitantly. This has subsided with reduction of the Capastat Sulfate dosage to 2 or 3 g per week.

Intravenously may be used. In mice the subcutaneous median lethal dose in mice was 514 mg/kg.

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