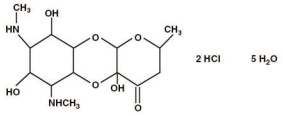
TROBICIN - spectinomycin
Pharmacia and Upjohn, Co.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of TROBICIN Sterile Powder and other antibacterial drugs, TROBICIN Sterile Powder should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.
For intramuscular Injection

DESCRIPTION
TROBICIN Sterile Powder contains spectinomycin hydrochloride which is an aminocyclitol antibiotic produced by a species of soil microorganism designated as *Streptomyces spectabilis*. Sterile spectinomycin hydrochloride is the pentahydrated dihydrochloride salt of spectinomycin. The structural formula is represented below:



Spectinomycin hydrochloride is isolated as a white to pale buff crystalline dihydrochloride pentahydrate powder, molecular weight 495, and is stable in the dry state for 36 months.

CLINICAL PHARMACOLOGY
TROBICIN Sterile Powder is rapidly absorbed after intramuscular injection. A single, two-gram injection produces peak serum concentrations averaging about 100 mcg/mL at one hour; a single, four-gram injection produces peak serum concentrations averaging 160 mcg/mL at two hours. Average serum concentrations of 15 mcg/mL for the two-gram dose and 31 mcg/mL for the four-gram dose were present eight hours after dosing.

Microbiology
Spectinomycin hydrochloride is an inhibitor of protein synthesis in the bacterial cell; the site of action is the 30S ribosomal subunit.
In vitro studies have shown spectinomycin hydrochloride to be active against most strains of *Neisseria gonorrhoeae* (minimum inhibitory concentration <7.5 to 20 mcg/mL).
Definitive *in vitro* studies have shown no cross-resistance of *N. gonorrhoeae* between spectinomycin hydrochloride and penicillin.
The antibiotic is not significantly bound to plasma protein.

INDICATIONS AND USAGE
TROBICIN Sterile Powder is indicated in the treatment of acute gonorrheal urethritis and proctitis in the male and acute gonorrheal cervicitis and proctitis in the female when due to susceptible strains of *Neisseria gonorrhoeae*. Men and women with known recent exposure to gonorrhea should be treated as those known to have gonorrhea.
The *in vitro* susceptibility of *Neisseria gonorrhoeae* to spectinomycin hydrochloride can be tested by agar diluted methods. TROBICIN Susceptibility Powder is available for this purpose and its package insert should be consulted for details.
To reduce the development of drug-resistant bacteria and maintain the effectiveness of TROBICIN Sterile Powder and other antibacterial drugs, TROBICIN Sterile Powder 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
The use of TROBICIN Sterile Powder is contraindicated in patients previously found hypersensitive to it.

WARNINGS
Spectinomycin hydrochloride is not effective in the treatment of syphilis. Antibiotics used in high doses for short periods of time to treat gonorrhea may mask or delay the symptoms of incubating syphilis. Since the treatment of syphilis demands prolonged therapy with any effective antibiotic, patients being treated for gonorrhea should be closely observed clinically. All patients with gonorrhea should have a serologic test for syphilis at the time of diagnosis. Patients treated with spectinomycin hydrochloride should have a follow-up serologic test for syphilis after three months.
Contains benzyl alcohol. Benzyl alcohol has been reported to be associated with a fatal "Gasping Syndrome" in premature infants and an increased incidence of neurologic and other complications.

PRECAUTIONS
The usual precautions should be observed with atopic individuals.
The clinical effectiveness of TROBICIN Sterile Powder should be monitored to detect evidence of development of resistance by *Neisseria gonorrhoeae*.

Prescribing TROBICIN Sterile Powder 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 TROBICIN Sterile Powder should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When TROBICIN Sterile Powder 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 TROBICIN Sterile Powder or other antibacterial drugs in the future.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Genotoxicity of spectinomycin hydrochloride was evaluated in six assay test systems including two Ames tests, two micronucleus tests in mice, unscheduled DNA synthesis in rat primary hepatocytes, and a chromosomal aberration test in Chinese hamster ovary cells. Spectinomycin was not shown to be mutagenic or genotoxic in these tests.
No adverse effects on fertility or general reproductive performance were observed when spectinomycin was administered subcutaneously to rats at dose levels up to 300 mg/kg (equivalent to the recommended maximum human dose based on mg/m^2).
A three-generation reproduction study in rats administered spectinomycin hydrochloride orally at dose levels up to 400 mg/kg (equivalent to the recommended maximum human dose based on mg/m^2) produced no evidence of drug-induced toxicity during growth, gestation, or lactation periods of any parental generation. Pregnancy rates of the 400 mg/kg/day groups were consistently lower than those of the control groups. A histopathological examination of the testes and ovaries of the third generation animals was normal.

Pregnancy

Teratogenic Effects

Pregnancy Category B
Spectinomycin was not teratogenic or embryocidal when orally or subcutaneously administered to rats at doses of 300 mg/kg/day (equivalent to the recommended maximum human dose based on mg/m^2). No teratogenic effects were observed when spectinomycin was administered intraperitoneally to mice or rats at dose levels of 400 or 1600 mg/kg/day, respectively. Spectinomycin was administered intramuscularly or subcutaneously to pregnant rabbits at dose levels up to 300 mg/kg/day (equivalent to the recommended maximum human dose based on mg/m^2). Embryonic and fetal development were unaffected by treatment. Since there are no controlled studies of spectinomycin in pregnant women, and because animal reproduction studies are not always predictive of human responses, spectinomycin should be used during pregnancy only if clearly needed.

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 spectinomycin is administered to a nursing woman.

Pediatric Use
Safety and effectiveness in the pediatric population have not been established. (See **WARNINGS**.)

ADVERSE REACTIONS
The following reactions were observed during the single dose clinical trials: soreness at the injection site, urticaria, dizziness, nausea, chills, fever and insomnia.
During multiple dose subchronic tolerance studies in normal human volunteers, the following were noted: a decrease in hemoglobin, hematocrit and creatinine clearance; elevation of alkaline phosphatase, BUN and SGPT. In single and multiple dose studies in normal volunteers, a reduction in urine output was noted. Extensive renal function studies demonstrated no consistent changes indicative of renal toxicity.
A few cases of anaphylaxis or anaphylactoid reactions have been reported. If serious allergic reactions occur, the usual agents (epinephrine, corticosteroids, and/or antihistamines) should be available for emergency use. In cases of severe anaphylaxis, airway support and oxygen may also be required.

OVERDOSAGE
Information on overdosage in humans is not available. Hemodialysis has been reported to aid in the removal of **intravenously administered** spectinomycin from the body.
Kusumi R, Metzler C, Fass R; Pharmacokinetics of Spectinomycin in Volunteers with Renal Insufficiency, *Chemotherapy*, 27:95–98 (1981).

DOSAGE AND ADMINISTRATION

Preparation of Drug for Intramuscular Injection

TROBICIN Sterile Powder, 2 grams: reconstitute with 3.2 mL of the accompanying diluent.[1]
Shake vials vigorously immediately after adding diluent and before withdrawing dose. It is recommended that disposable syringes and needles be used to avoid contamination with penicillin residue, especially when treating patients known to be highly sensitive to penicillin. **Use of a 20-gauge needle is recommended.**

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1Bacteriostatic Water for Injection with Benzyl Alcohol 0.945% w/v added as preservative.

Dosage

Intramuscular injections should be made deep into the upper outer quadrant of the gluteal muscle.
Adults (Men and Women)—Inject 5 mL intramuscularly for a 2-gram dose. This is also the recommended dose for patients being treated after failure of previous antibiotic therapy.
In geographic areas where antibiotic resistance is known to be prevalent, initial treatment with 4 grams (10 mL) intramuscularly is preferred. The 10-mL injection may be divided between two gluteal injection sites.

STORAGE CONDITIONS

Store unreconstituted product at controlled room temperature 20° to 25°C (68° to 77°F) [see USP]. Store prepared suspension at controlled room temperature 20° to 25°C (68° to 77°F) and use within 24 hours.

HOW SUPPLIED

Contains benzyl alcohol. (See **WARNINGS**.)
TROBICIN Sterile Powder is available as:
TROBICIN Sterile Powder, 2-gram vial NDC 0009-0566-01—with one ampoule of Bacteriostatic Water for Injection with Benzyl Alcohol 0.945% w/v added as preservative. When reconstituted with 3.2 mL of the accompanying diluent, each vial yields a sufficient quantity for withdrawal of 5 mL of a suspension containing 400 mg spectinomycin per mL (as the hydrochloride). Five mL provides 2 grams spectinomycin. For intramuscular use only.
TROBICIN Susceptibility Powder—100 mg. See package insert for *in vitro* testing procedure.

Rx only

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