LESHCUTAN®

OINTMENT

Composition

Active Ingredients

Paromomycin (as sulfate)	15%
Methylbenzethonium chloride	12%

Other Ingredients
Light liquid paraffin, white vaseline.

Action

Leshcutan is a dermatological preparation intended for the topical treatment of cutaneous leishmaniasis.

Paromomycin is an aminoglycoside antibiotic produced by the growth of certain strains of *Streptomyces rimosus* var *paromomycinus.* It has an antimicrobial spectrum similar to that of neomycin sulfate. There is cross-resistance between paromomycin, neomycin, framycetin, kanamycin, and streptomycin.

Paromomycin administered orally has for many years been used for the treatment of both acute and chronic intestinal amebiasis, in the suppression of intestinal flora, both preoperatively and in the management of hepatic coma.

Methylbenzethonium chloride is a quaternary ammonium compound with antimicrobial activity. It is widely used as a topical anti-infective and also as a preservative and cationic surfactant in a variety of pharmaceutical and cosmetic preparations.

Pharmacodynamics

Paromomycin, like all the aminoglycoside antibiotics, inhibits protein biosynthesis in sensitive organisms.

Electron microscopy studies indicated that the main organelles of promastigotes and amastigotes affected by Leshcutan are the mitochondria by methylbenzethonium chloride and the reticular system by paromomycin.

Paromomycin was studied *in vitro* on *Leishmania major* amastigotes cultured in C_3H/He mouse peritoneal exudate cells. The therapeutic activity, expressed as the minimum effective concentration which reduced the parasite survival index by 50% after 48 hours exposure to paromomycin, was 10 μg/ml.

Methylbenzethonium chloride was reported to decrease the growth of *Leishmania major* promastigotes and amastigotes *in vitro.*

The effect of different concentrations of paromomycin with various percentages of methylbenzethonium chloride on the development of *Leishmania major* in BALB/c and C_3H/He mice was studied. Ointments containing either paromomycin alone or methylbenzethonium chloride alone had only a partial effect on the parasites.

The in vivo efficacy of Leshcutan containing 15% paromomycin and 12% methylbenzethonium chloride against experimentally-induced cutaneous leishmaniasis in BALB/c and C_3H/He mice demonstrated a 100% cure rate in mice inoculated with *L. major* and *L. mexicana.*

Pharmacokinetics

Paromomycin is poorly absorbed after oral therapy. However, following intramuscular injection of single and multiple injections of paromomycin, peak serum levels occur within the first 2 hours, followed by a rapid fall of drug concentration in the serum and the appearance of high concentrations of the drug in the urine. The half-life of serum antibiotic activity is approximately 5 hours. No local or systemic toxic reactions attributable to the drug were observed, nor was there any evidence of accumulation of the drug in the body in the presence of normal renal function. In the presence of an abnormal kidney, excretion of paromomycin may be hindered, therefore potential nephrotoxic symptoms might occur. Intramuscular injections of paromomycin do not seem to penetrate the blood-brain barrier.

The kinetics of paromomycin following topical application was examined using the microbiological inhibition zone method. Sera were collected from patients on the last day of a 10-day course of treatment at 1, 4 and 24 hours after termination of treatment with 15% paromomycin and 12% methylbenzethonium chloride. Bioassay using *Staphylococcus epidermitidis*, a test sensitive to 0.1 μg/ml of paromomycin, failed to detect the drug in the sera of treated patients at any time point tested.

Clinical Studies

In a clinical study, 67 patients with cutaneous leishmaniasis caused by *Leishmania major* were treated topically twice daily with Leshcutan. After 10 days, 73% of the patients had no parasites in their lesions, 14% became free within a further 20 days without further treatment, and 13% failed to respond. Clinical healing was generally complete within 10 to 30 days of treatment; 94% of the treated lesions healed with little or no scarring.

In another study, 30 patients were treated with Leshcutan for 10 days in a randomized, double-blind, crossover study. The cure rate was 77% (23 out of 30 patients) immediately following treatment with delayed clearing of 10 days in an additional 2 patients (6%). The spontaneous cure rate in 11 patients receiving placebo was 18% (2 patients cured). At the end of treatment with Leshcutan, parasites were eliminated only from the treated lesion while the untreated control lesion(s) of the same patient contained living parasites.

Indications

Topical treatment of cutaneous leishmaniasis.

Contraindications

Known hypersensitivity to any of the components of the preparation.

The preparation is not intended for ophthalmic use nor should it be applied in the external auditory canal of patients with perforated eardrum.

Warnings

Leshcutan should not be used over a wide area or for extended periods of time, because of the risk of nephrotoxicity and ototoxicity associated with aminoglycoside antibiotics.

Use in Pregnancy

Safety of use in pregnancy has not been established.

Use in Breastfeeding

Safety of use in breastfeeding has not been established.

Adverse Reactions

Leshcutan may cause redness, irritation, local inflammation, local burning sensation, erythema, edema, local pain and contact dermatitis. These reactions generally subside after 2-3 days of use and do not interfere with the therapeutic activity of the ointment.

Allergic cross-reactions may occur which could prevent future use of any or all of the aminoglycoside antibiotics such as neomycin, framycetin, kanamycin, streptomycin, and particularly gentamicin.

Precautions

Caution should be exercised in the administration of Leshcutan to patients sensitive to neomycin.

Caution should be exercised in patients with renal, hepatic or hearing impairment because of possible accumulation of paromomycin, which is potentially nephrotoxic and ototoxic.

If unacceptably severe local reactions occur, treatment may be interrupted for 2-3 days and resumed after symptoms have subsided.

Directions for Use

The affected area should be cleaned. The ointment should completely cover the lesion. The lesion may then be covered with a sterile bandage.

The ointment should be applied twice daily for a period of 10 days. If complete healing has not occurred after 10 days of therapy, an additional 10-day course of treatment may be recommended.

If unacceptable severe local reactions occur, treatment may be interrupted for 2-3 days and resumed after symptoms have subsided.

Manufacturer

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