DESCRIPTION
Cortisporin®-TC Otic Suspension with Neomycin and Hydrocortisone (colistin sulfate—neomycin sulfate—thrombomycin bromide—hydrocortisone acetate otic suspension) is a sterile antibacterial and anti-inflammatory aqueous suspension containing in each mL: Colistin base activity, 3 mg (as the sulfate); Neomycin base activity, 3.3 mg (as the sulfate); Hydrocortisone acetate, 10 mg (1%); Thrombomycin bromide, 0.5 mg (0.05%); Polysorbate 80, acetic acid, and sodium acetate in a buffered aqueous vehicle. Thermostable (mercury derivati- ve), 0.002%, is added as a preservative. It is a nonviscous, buffered at pH 5, for instillation into the canal of the external ear or direct application to the affected aural skin.

The structural formulas of colistin sulfate (mixture of Colistin A & B), neomycin sulfate (mixture of neomycin A, B, & C), hydrocortisone acetate ((11β,21)-21-acetoxy-11,17-dihydroxyprogynyl methyl-2 pyrimidylaminolato) ethyl), N,N-dimethyl-1-hexadecanaminium, bromide) are represented below:

INDICATIONS AND USAGE
Cortisporin®-TC Otic Suspension with Neomycin and Hydrocortisone is indicated for the treatment of superficial bacterial infections of the external auditory canal, caused by organisms susceptible to the action of the antibiotics; and for the treatment of infections of mastoidectomy and fenestration cavities has been demonstrated in a controlled clinical trial.

Susceptibility Tests:
In vitro and in clinical infections as described in the INDICATIONS AND USAGE section.

CLINICAL PHARMACOLOGY
Colistin sulfate is a polyene antibiotic which penetrates into and disrupts the bacterial cell membrane. Neomycin sulfate is an aminoglycoside antibiotic which inhibits protein synthesis, disrupting the normal cycle of ribosomal function. Hydrocortisone acetate is a corticosteroid hormone which is thought to act by regulating the rate of protein synthesis; it causes inflammation, edema, pruritus and other dermal reactions. Corticosteroids suppress the inflammatory response to a variety of agents and they may delay healing. Since corticoids may inhibit the body’s defense mechanism against infection, a concomitant antimicrobial drug may be used when this inhibition is considered to be clinically significant in a particular case.

The relative potency of corticosteroids depends on the molecular structure, concentration, and release from the vehicle. Thrombomycin bromide is a surface-active agent that promotes tissue contact by dispersion and penetration of the cellular debris and exudate.

Microbiology:
Together, colistin sulfate and neomycin sulfate have bactericidal activity against most strains of the following microorganisms, both in vitro and in clinical infections as described in the INDICATIONS AND USAGE section.

Aerobic gram-positive microorganisms:
Staphylococcus aureus.

Aerobic gram-negative microorganisms:
Enterobacter aerogenes
Escherichia coli
Klebsiella pneumoniae
Pseudomonas aeruginosa.

Susceptibility Tests:
It is not recommended that colistin sulfate or neomycin sulfate be routinely tested and reported by clinical microbiology laboratories.

INDICATIONS AND USAGE
Cortisporin®-TC Otic Suspension is indicated for the treatment of superficial bacterial infections of the external auditory canal, caused by organisms susceptible to the action of the antibiotics; and for the treatment of infections of mastoidectomy and fenestration cavities, caused by organisms susceptible to the antibiotics.

CONTRAINDICATIONS
This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

This product should not be used if the external auditory canal disorder is suspected or known to be due to cutaneous viral infection (e.g., herpes simplex virus or varicella zoster virus).

WARNINGS
Neomycin can induce permanent sensorineural hearing loss due to cochlear damage, mainly destruction of hair cells in the organ of Corti. The risk is greater with prolonged use. Therapy should be limited to 10 consecutive days. (See PRECAUTIONS-General.) Patients being treated with eardrops containing neomycin should be under close clinical observation. Cortisporin®-TC Otic Suspension should be used cautiously in any patient with a perforated tympanic membrane.

Neomycin sulfate may cause cutaneous sensitization. A precise incidence of hypersensitivity reactions (primarily skin rash) due to topical neomycin is usually a low-grade reddening with swelling, dry scaling, and itching; more liable than is normal skin to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low-grade reddening with swelling, dry scaling, and itching; it may be manifested simply as a failure to heal. Patch examination for such signs is advisable, and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin containing applications should be avoided for the patient thereafter.

PRECAUTIONS
General
As with any other antibiotic preparation, prolonged treatment may result in overgrowth of nonsusceptible organisms (e.g., fungi). If the infection is not improved after one week, cultures should be repeated to verify the identity of the organism and to determine whether therapy should be changed.

Corticosteroids should not be used beyond 10 days, and then only if indicated.

Allergic cross-reactions may occur which could prevent the use of any or all of the aminoglycoside antibiotics for the treatment of future infections.

Information for Patients
Avoid contaminating the dropper with material from the ear, fingers, or other source. This caution is necessary if sensitization or irritation occurs, discontinue use immediately and contact your physician.

Do not use in the eyes.

If the infection is not improved after one week, cultures should be repeated to verify the diagnosis.

Laboratory Tests

Systemic effects of excessive levels of hydrocortisone may include a reduction in the number of circulating eosinophils and a decrease in urinary excretion of T-4 hydrocortisone.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term animal carcinogenicity studies have not been performed with colistin or neomycin, or Cortisporin®-TC Otic Suspension. An increased incidence of chromosome aberrations in human lymphocytes has been reported following in vitro exposure to colistin or neomycin.

Fertility studies have not been performed with neomycin, but reports from the scientific literature suggest that it may decrease spermatogenesis in rats. No adverse effects on fertility were observed in male or female rats given intramuscular injections of colistimethate sodium; the methanesulfonate salt of colistin, up to 20 mg/kg (equivalent to 9.3 mg/kg of colistin base). This is approximately 30 times the daily dose based on body surface area, assuming 100% absorption from the ear; however, significant systemic levels of colistin or neomycin would not be anticipated in humans when Cortisporin®-TC Otic Suspension is used as directed.

Long term studies in rodents showed no evidence of carcinogenicity attributable to oral administration of corticosteroids. Mutagenicity studies with hydrocortisone were negative. Studies have not been performed to evaluate the effect on fertility of topical corticosteroids.

Pregnancy-Teratogenic Effects

Pregnancy Category C – There are no adequate and well controlled studies of Cortisporin®-TC Otic Suspension in pregnant women. It is not known whether Cortisporin®-TC Otic Suspension can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, no adverse effects on fertility of topical corticosteroids have been show to be teratogenic after dermal application in laboratory animals. Cortisporin®-TC Otic Suspension should be used during pregnancy only if the potential benefit justifies the possible risk to the fetus.

Nursing Mothers:
Hydrocortisone and colistin sulfate appear in human milk following oral administration of the drugs. Since systemic absorption of these drugs may occur when they are used topically, caution should be exercised when Cortisporin®-TC Otic Suspension is used by a nursing woman.

Pediatric Use: See DOSAGE AND ADMINISTRATION

ADMINISTRATION
The safety and effectiveness of Cortisporin®-TC Otic Suspension in infants below one year of age have not been established. The use of Cortisporin®-TC Otic Suspension in pediatric patients one year or older in the treatment of superficial bacterial infections of the external auditory canal and for the treatment of infections of mastoidectomy and fenestration cavities has been demonstrated in a controlled clinical trial.

Geriatric Use:
No overall differences in safety or effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS
Neomycin occasionally causes skin sensitization. Ototoxicity (see WARNINGS section) and nephrotoxicity have also been reported. Adverse reactions have occurred with topical use of antibiotic combinations. Exact incidence figures are not available. The most frequently reported adverse effects with Cortisporin®-TC Otic Suspension are local reactions. When using the calibrated dropper:

For adults, 5 drops of the suspension should be instilled into the affected ear 3 or 4 times daily. For pediatric patients, 4 drops should be instilled into the affected ear 3 or 4 times daily. For pediatric patients, 4 drops are suggested because of the smaller capacity of the ear canal.

The patient should lie with the affected ear upward and then the drops should be instilled. This position should be maintained for 5 minutes to facilitate penetration of the drops into the ear canal. Repeat, if necessary, for the opposite ear.

If preferred, a cotton wick may be inserted into the canal and then the cotton may be saturated with the suspension. This wick should be kept moist by adding further solution every 4 hours. The wick should be replaced at least once every 24 hours.

HOW SUPPLIED
Cortisporin®-TC Otic Suspension is supplied as: NDC 42023-109-01
10 mL bottle with dropper cap assembly and 0.002% mercuric chloride. Colistin sulfate equivalent to 3 mg of colistin base activity, Neomycin sulfate equivalent to 3.3 mg of neomycin base activity, Hydrocortisone acetate 10 mg (1%), Thonzonium bromide 0.5 mg (0.05%), and Polysorbate 80 in an aqueous vehicle buffered with acetic acid and sodium acetate. Thermostable (mercury derivative) 0.002% is added as a preservative.

A sterilized dropper-cap assembly for use on the bottle of suspension is included in the package. Store the bottle out of reach of children.

SHAKE WELL BEFORE USING.

Store between 20° to 25°C (68° to 77°F). (See USP Controlled Room Temperature.) Rx only.

Distributed by:
Par Pharmaceutical Companies, Inc.
Chestnut Ridge, NY 10977

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