**CIPROFLOXACIN HYDROCHLORIDE AND HYDROCORTISONE- ciprofloxacin hydrochloride and hydrocortisone suspension/ drops**
**Cosette Pharmaceuticals, Inc.**

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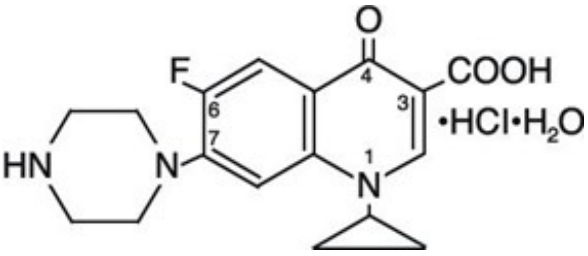
**Ciprofloxacin Hydrochloride and Hydrocortisone Otic Suspension**

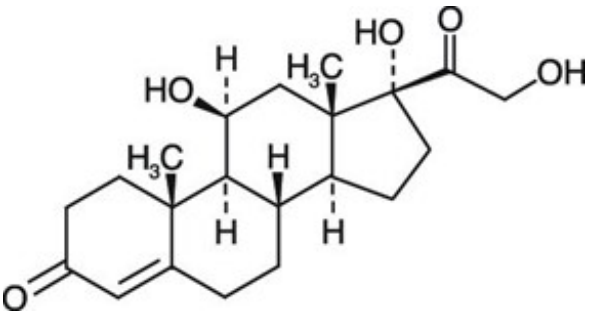
## DESCRIPTION

Ciprofloxacin hydrochloride and hydrocortisone otic suspension contains the synthetic broad spectrum antibacterial agent, ciprofloxacin hydrochloride, combined with the anti-inflammatory corticosteroid, hydrocortisone, in a preserved, nonsterile suspension for otic use. Each mL of ciprofloxacin hydrochloride and hydrocortisone otic suspension contains ciprofloxacin hydrochloride (equivalent to 2 mg ciprofloxacin), 10 mg hydrocortisone, and 9 mg benzyl alcohol as a preservative. The inactive ingredients are glacial acetic acid, phospholipon 90H (modified lecithin), polysorbate, polyvinyl alcohol, purified water, sodium acetate, and sodium chloride. Sodium hydroxide or hydrochloric acid may be added for adjustment of pH.

Ciprofloxacin, a fluoroquinolone, is available as the monohydrochloride monohydrate salt of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid. Its empirical formula is $C_{17}H_{18}FN_3O_3 \cdot HCl \cdot H_2O$ and its chemical structure is as follows:




Hydrocortisone, pregn-4-ene-3, 20-dione, 11, 17, 21-trihydroxy-(11β)-, is an anti-inflammatory corticosteroid. Its empirical formula is $C_{21}H_{30}O_5$ and its chemical structure is:




## CLINICAL PHARMACOLOGY

The plasma concentrations of ciprofloxacin were not measured following three drops of otic suspension administration because the systemic exposure to ciprofloxacin is expected to be below the limit of quantitation of the assay (0.05 µg/mL).

Similarly, the predicted $C_{max}$ of hydrocortisone is within the range of endogenous hydrocortisone concentration (0-150 ng/mL), and therefore can not be differentiated from the endogenous cortisol.

Preclinical studies have shown that ciprofloxacin hydrochloride and hydrocortisone otic suspension was not toxic to the guinea pig cochlea when administered intratympanically twice daily for 30 days and was only weakly irritating to rabbit skin upon repeated exposure.

Hydrocortisone has been added to aid in the resolution of the inflammatory response accompanying bacterial infection.

**Microbiology**

Ciprofloxacin has *in vitro* activity against a wide range of gram-positive and gram-negative microorganisms. The bactericidal action of ciprofloxacin results from interference with the enzyme, DNA gyrase, which is needed for the synthesis of bacterial DNA. Cross-resistance has been observed between ciprofloxacin and other fluoroquinolones. There is generally no cross-resistance between ciprofloxacin and other classes of antibacterial agents such as beta-lactams or aminoglycosides.

Ciprofloxacin has been shown to be active against most strains of the following microorganisms, both *in vitro* and in clinical infections of acute otitis externa as described in the **INDICATIONS AND USAGE** section:

**Aerobic gram-positive microorganism**

*Staphylococcus aureus*

**Aerobic gram-negative microorganisms**

*Proteus mirabilis*

*Pseudomonas aeruginosa*

## INDICATIONS AND USAGE

Ciprofloxacin hydrochloride and hydrocortisone otic suspension is indicated for the treatment of acute otitis externa in adult and pediatric patients, one year and older, due to susceptible strains of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Proteus mirabilis*.

## CONTRAINDICATIONS

Ciprofloxacin hydrochloride and hydrocortisone otic suspension is contraindicated in persons with a history of hypersensitivity to hydrocortisone, ciprofloxacin or any member of the quinolone class of antimicrobial agents. This nonsterile product should not be used if the tympanic membrane is known or suspected to be perforated. Use of this product is contraindicated in viral infections of the external canal including varicella and herpes simplex infections.

## WARNINGS

**NOT FOR OPHTHALMIC USE. NOT FOR INJECTION.**

Ciprofloxacin hydrochloride and hydrocortisone otic suspension should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity. Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving systemic quinolones. Serious acute hypersensitivity reactions may require immediate emergency treatment. The dropper cap contains natural rubber (latex) which may cause severe allergic reactions.

## PRECAUTIONS

### GENERAL:

As with other antibiotic preparations, use of this product may result in overgrowth of nonsusceptible organisms, including fungi. If the infection is not improved after one week of therapy, cultures should be obtained to guide further treatment.

### Information for Patients:

If rash or allergic reaction occurs, discontinue use immediately and contact your physician.

Do not use in the eyes.

Avoid contaminating the dropper with material from the ear, fingers, or other sources.

Protect from light.

Shake well immediately before using.

Discard unused portion after therapy is completed.

### Carcinogenesis, Mutagenesis, Impairment of Fertility:

Eight *in vitro* mutagenicity tests have been conducted with ciprofloxacin, and the test results are listed below:

Salmonella/Microsome Test (Negative)

*E. coli* DNA Repair Assay (Negative)

Mouse Lymphoma Cell Forward Mutation Assay (Positive)

Chinese Hamster V79 Cell HGPRT Test (Negative)

Syrian Hamster Embryo Cell Transformation Assay (Negative)

*Saccharomyces cerevisiae* Point Mutation Assay (Negative)

*Saccharomyces cerevisiae* Mitotic Crossover and Gene Conversion Assay (Negative)

Rat Hepatocyte DNA Repair Assay (Positive)

Thus, 2 of the 8 tests were positive, but results of the following 3 in vivo test systems gave negative results:

Rat Hepatocyte DNA Repair Assay

Micronucleus Test (Mice)

Dominant Lethal Test (Mice)

Long-term carcinogenicity studies in mice and rats have been completed for ciprofloxacin. After daily oral doses of 750 mg/kg (mice) and 250 mg/kg (rats) were administered for up to 2 years, there was no evidence that ciprofloxacin had any carcinogenic or tumorigenic effects in these species. No long term studies of ciprofloxacin hydrochloride and hydrocortisone otic suspension have been performed to evaluate carcinogenic potential.

Fertility studies performed in rats at oral doses of ciprofloxacin up to 100 mg/kg/day revealed no evidence of impairment. This would be over 1000 times the maximum recommended clinical dose of ototopical ciprofloxacin based upon body surface area, assuming total absorption of ciprofloxacin from the ear of a patient treated with ciprofloxacin hydrochloride and hydrocortisone otic suspension twice per day.

Long term studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical hydrocortisone. Mutagenicity studies with hydrocortisone were negative.

**Pregnancy: Teratogenic Effects:**

Reproduction studies have been performed in rats and mice using oral doses of up to 100 mg/kg and IV doses up to 30 mg/kg and have revealed no evidence of harm to the fetus as a result of ciprofloxacin. In rabbits, ciprofloxacin (30 and 100 mg/kg orally) produced gastrointestinal disturbances resulting in maternal weight loss and an increased incidence of abortion, but no teratogenicity was observed at either dose. After intravenous administration of doses up to 20 mg/kg, no maternal toxicity was produced in the rabbit, and no embryotoxicity or teratogenicity was observed.

Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals.

Animal reproduction studies have not been conducted with ciprofloxacin hydrochloride and hydrocortisone otic suspension. No adequate and well controlled studies have been performed in pregnant women. Caution should be exercised when ciprofloxacin hydrochloride and hydrocortisone otic suspension is used by a pregnant woman.

**Nursing Mothers:**

Ciprofloxacin is excreted in human milk with systemic use. It is not known whether ciprofloxacin is excreted in human milk following topical otic administration. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

**Pediatric use:**

The safety and efficacy of ciprofloxacin hydrochloride and hydrocortisone otic suspension have been established in pediatric patients 2 years and older (131 patients) in adequate and well-controlled clinical trials. Efficacy has been extrapolated for patients, age 1 year and above based on studies in adults and older pediatric patients.

## ADVERSE REACTIONS

In Phase 3 clinical trials, a total of 564 patients were treated with ciprofloxacin hydrochloride and hydrocortisone otic suspension. Adverse events with at least remote relationship to treatment included headache (1.2%) and pruritus (0.4%). The following treatment-related adverse events were each reported in a single patient: migraine, hypesthesia, paresthesia, fungal dermatitis, cough, rash, urticaria, and alopecia.

The following reactions have been identified during post-approval use of ciprofloxacin hydrochloride and hydrocortisone otic suspension in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to ciprofloxacin hydrochloride and hydrocortisone otic suspension, or a combination of these factors include: dizziness, ear canal erythema, ear congestion, hypoacusis and medication residue.

**To report SUSPECTED ADVERSE REACTIONS, contact Cosette Pharmaceuticals, Inc. at 1-800-922-1038 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.**

## DOSAGE AND ADMINISTRATION

SHAKE WELL IMMEDIATELY BEFORE USING.

For children (age 1 year and older) and adults, 3 drops of the suspension should be instilled into the affected ear twice daily for seven days. The suspension should be warmed by holding the bottle in the hand for 1-2 minutes to avoid the dizziness which may result from the instillation of a cold solution into 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 30-60 seconds to facilitate penetration of the drops into the ear. Repeat, if necessary, for the opposite ear. Discard unused portion after therapy is completed.

## HOW SUPPLIED

Ciprofloxacin hydrochloride and hydrocortisone otic suspension is supplied as a white to off-white opaque suspension in a 10 mL bottle with a dropper dispenser:

NDC 0713-0851-09

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Avoid freezing. Protect from light.

**Distributed by:**
Cosette Pharmaceuticals NC Laboratories, LLC
Lincolnton, NC 28092

8-0851CPLNC1
Revised: 02/2025
VC7789

**PRINCIPAL DISPLAY PANEL**

NDC 0713- **0851**-09

**Rx only**

**Ciprofloxacin Hydrochloride 0.2% and Hydrocortisone 1% Otic Suspension**

**For use in ears only**

**10 mL**

**Cosette Pharmaceuticals NC Laboratories, LLC**


## CIPROFLOXACIN HYDROCHLORIDE AND HYDROCORTISONE

ciprofloxacin hydrochloride and hydrocortisone suspension/ drops

| Product Information |
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|---|---|---|---|
| **Product Type** | HUMAN PRESCRIPTION DRUG | **Item Code (Source)** | NDC:0713-0851 |
| **Route of Administration** | AURICULAR (OTIC) | | |

## Active Ingredient/Active Moiety

| Ingredient Name | Basis of Strength | Strength |
|---|---|---|
| **CIPROFLOXACIN HYDROCHLORIDE** (UNII: 4BA73M5E37) (CIPROFLOXACIN - UNII:5E8K9I0O4U) | CIPROFLOXACIN | 2 mg in 1 mL |
| **HYDROCORTISONE** (UNII: WI4X0X7BPJ) (HYDROCORTISONE - UNII:WI4X0X7BPJ) | HYDROCORTISONE | 10 mg in 1 mL |

## Inactive Ingredients

| Ingredient Name | Strength |
|---|---|
| **POLYVINYL ALCOHOL** (UNII: 532B59J990) | |
| **SODIUM CHLORIDE** (UNII: 451W47IQ8X) | |
| **SODIUM ACETATE** (UNII: 4550K0SC9B) | |
| **ACETIC ACID** (UNII: Q40Q9N063P) | |
| **LECITHIN, SOYBEAN** (UNII: 1DI56QDM62) | |
| **POLYSORBATE 20** (UNII: 7T1F30V5YH) | |
| **WATER** (UNII: 059QF0KO0R) | |
| **SODIUM HYDROXIDE** (UNII: 55X04QC32I) | |
| **HYDROCHLORIC ACID** (UNII: QTT17582CB) | |
| **BENZYL ALCOHOL** (UNII: LKG8494WBH) | |

## Packaging

| # | Item Code | Package Description | Marketing Start Date | Marketing End Date |
|---|---|---|---|---|
| **1** | NDC:0713-0851-09 | 1 in 1 CARTON | 12/04/2025 | |
| **1** | | 10 mL in 1 BOTTLE; Type 0: Not a Combination Product | | |

## Marketing Information

| Marketing Category | Application Number or Monograph Citation | Marketing Start Date | Marketing End Date |
|---|---|---|---|
| ANDA | ANDA218273 | 12/04/2025 | |

## Labeler - Cosette Pharmaceuticals, Inc. (116918230)

## Establishment

| Name | Address | ID/FEI | Business Operations |
|---|---|---|---|
| Cosette Pharmaceuticals NC Laboratories, LLC | | 079419931 | label(0713-0851) , manufacture(0713-0851) , pack(0713-0851) , analysis(0713-0851) |