CIPROFLOXACIN OTIC- ciprofloxacin solution/ drops
Genus Lifesciences

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use CIPROFLOXACIN OTIC SOLUTION safely and effectively. See full prescribing information for CIPROFLOXACIN OTIC SOLUTION

CIPROFLOXACIN otic solution
Initial U.S. Approval: 1987

INDICATIONS AND USAGE

Ciprofloxacin otic solution, 0.2% is a quinolone antimicrobial indicated for the treatment of acute otitis externa due to susceptible isolates of *Pseudomonas aeruginosa* or *Staphylococcus aureus*. (1)

DOSAGE AND ADMINISTRATION

Contents of one single-dose container should be instilled into the affected ear twice daily (approximately 12 hours apart) for 7 days. (2)

DOSAGE FORMS AND STRENGTHS

Ciprofloxacin otic solution, 0.2% is a sterile, preservative-free otic solution of ciprofloxacin hydrochloride equivalent to 0.2 % ciprofloxacin (0.5 mg in 0.25 mL) in each single-dose container. (3)

CONTRAINDICATIONS

History of hypersensitivity to ciprofloxacin. (3)

WARNINGS AND PRECAUTIONS

Ciprofloxacin otic solution, 0.2% is for otic use only. (5.1)
Hypersensitivity: discontinue at the first appearance of a skin rash or any other sign of hypersensitivity. (5.2)
Use of ciprofloxacin otic solution, 0.2% may result in overgrowth of nonsusceptible organisms. (5.3)

ADVERSE REACTIONS

The most common adverse reactions reported in 2-3% of patients treated with ciprofloxacin otic solution, 0.2% were application site pain, ear pruritus, fungal ear superinfection and headache. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Allucent at 1-866-511-6754 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*. (6)
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 12/2024

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Ciprofloxacin otic solution, 0.2% is a quinolone antimicrobial indicated for the treatment of acute otitis externa due to susceptible isolates of *Pseudomonas aeruginosa or Staphylococcus aureus*.

2 DOSAGE AND ADMINISTRATION

The contents of one single-dose container (deliverable volume: 0.25 mL) should be instilled into the affected ear twice daily (approximately 12 hours apart) for 7 days.

Wash hands before use. The solution should be warmed, by holding the container in the hands for at least 1 minute, to minimize the dizziness that 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 solution should be instilled. This position should be maintained for at least 1 minute to facilitate penetration of the drops into the ear. Repeat, if necessary, for the opposite ear. Discard unused portion.

3 DOSAGE FORMS AND STRENGTHS

Ciprofloxacin otic solution, 0.2% is a sterile, preservative-free, otic solution of ciprofloxacin hydrochloride equivalent to 0.2 % ciprofloxacin (0.5 mg in 0.25 mL) in each single-dose container.

4 CONTRAINDICATIONS

Ciprofloxacin otic solution, 0.2% is contraindicated in persons with a history of

hypersensitivity to ciprofloxacin.

5 WARNINGS AND PRECAUTIONS

5.1 Otic Use Only

Ciprofloxacin otic solution, 0.2% is for otic use only. It should not be used for injection, for inhalation or for topical ophthalmic use.

5.2 Hypersensitivity

Ciprofloxacin otic solution, 0.2% should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity.

5.3 Growth of Rsistant Organisms with Prolonged Use

As with other anti-infectives, use of ciprofloxacin otic solution, 0.2% may result in overgrowth of nonsusceptible organisms, including yeast and fungi. If super-infection occurs, discontinue use and institute alternative therapy.

5.4 Lack of Clinical Response

If the infection is not improved after one week of therapy, cultures may help guide further treatment.

6 ADVERSE REACTIONS

Because clinical studies are conducted under widely varying conditions, adverse drug reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in clinical practice.

In a randomized, active-controlled clinical trial, approximately 300 patients with clinical signs and symptoms of otitis externa were treated with ciprofloxacin otic solution, 0.2%. The most frequently reported adverse reactions were application site pain, ear pruritus, fungal ear superinfection, and headache, each reported in approximately 2-3% of patients.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C.

Reproduction studies have been performed in rats and mice using oral doses of up to 100 mg/kg and intravenous (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.

Animal reproduction studies have not been conducted with ciprofloxacin otic solution, 0.2%. No adequate and well controlled studies have been performed in pregnant women. Caution should be exercised when ciprofloxacin otic solution, 0.2% is used by a pregnant woman.

8.3 Nursing Mothers

Ciprofloxacin is excreted in human milk with systemic use. It is not known whether ciprofloxacin is excreted in human milk following otic use. 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.

8.4 Pediatric Use

The safety and effectiveness of ciprofloxacin otic solution, 0.2% in infants below one year of age have not been established. The efficacy of ciprofloxacin otic solution, 0.2% in treating otitis externa in pediatric patients one year or older has been demonstrated in controlled clinical trials (see Section 14 Clinical Studies).

There is no evidence that the otic administration of quinolones has any effect on weight bearing joints, even though systemic administration of some quinolones has been shown to cause arthropathy in immature animals.

8.5 Geriatric Use

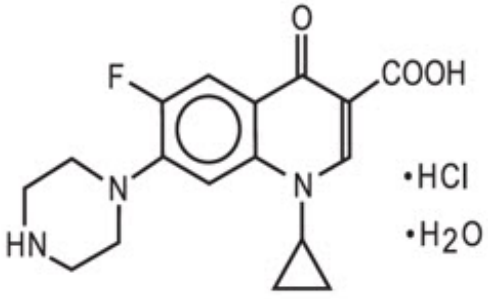
No overall differences in safety and effectiveness have been observed between elderly and younger patients.

11 DESCRIPTION

Ciprofloxacin otic solution, 0.2% contains the synthetic antimicrobial agent ciprofloxacin hydrochloride. Ciprofloxacin otic solution, 0.2% is a sterile, preservative-free solution for otic use. Each single-dose container of ciprofloxacin otic solution, 0.2% delivers 0.25 mL of solution equivalent to 0.5 mg of ciprofloxacin. The inactive ingredients are povidone, glycerin, and water for injection. Sodium hydroxide and/or lactic acid may be added to adjust pH.

Ciprofloxacin, a fluroquinolone is available as the monohydrochloride, monohydrate salt of 1cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid. Its molecular formula is $C_{17}H_{18}FN_3O_3 \cdot HCl \cdot H_2O$, and molecular weight is 385.82.

The chemical structure of ciprofloxacin hydrochloride is:



12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Ciprofloxacin is a fluoroquinolone antimicrobial (see 12.4 Clinical Pharmacology, Microbiology).

12.3 Pharmacokinetics

The plasma concentrations of ciprofloxacin were not measured following administration of 0.25 mL ciprofloxacin otic solution, 0.2% (total dose: 0.5 mg ciprofloxacin). However, the maximum plasma concentration of ciprofloxacin is anticipated to be less than 5 ng/mL.

12.4 Microbiology

The bactericidal action of ciprofloxacin results from interference with the enzyme DNA gyrase, which is needed for the synthesis of bacterial DNA.

Bacterial resistance to quinolones can develop through chromosomally- or plasmid-mediated mechanisms.

The mechanism of action of fluoroquinolones, including ciprofloxacin, is different from that of macrolides. Therefore, ciprofloxacin may be active against pathogens that are resistant to these antibiotics, and these antibiotics may be active against pathogens that are resistant to ciprofloxacin. *In vitro* studies demonstrated cross-resistance between ciprofloxacin and some fluoroquinolones.

Ciprofloxacin has been shown to be active against most isolates of the following bacteria, both *in vitro* and in clinical infections of acute otitis externa as described in Section 1 Indications and Usage.

Staphylococcus aureus	*Pseudomonas aeruginosa*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility

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 otic solution, 0.2% have been performed to evaluate carcinogenic potential.

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

- *Salmonella/*Microsome Test (Negative)
- *Escherichia 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).

Two of the 8 *in vitro* 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).

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 100 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 otic solution, 0.2% twice per day.

14 CLINICAL STUDIES

In a randomized, multi-center, evaluator-blinded study of patients with acute otitis externa, patients were treated with either ciprofloxacin otic solution, 0.2% twice daily or neomycin and polymyxin B sulfates and hydrocortisone otic solution (PNH) three times daily for 7 days.

In the per protocol population, clinical cure was achieved at the end of a 7-day treatment in 70% (173/247) for the ciprofloxacin otic solution, 0.2% treated group versus 60% (147/243) for the control treated group.

16 HOW SUPPLIED/STORAGE AND HANDLING

Ciprofloxacin otic solution, 0.2% is a clear, colorless, sterile, preservative-free solution. Ciprofloxacin otic solution, 0.2% is supplied as a 0.2% otic solution in a low-density polyethylene (LDPE) single-dose container. Each single-dose container delivers 0.25 mL of solution equivalent to 0.5 mg of ciprofloxacin; 14 single-dose containers are packaged in a foil overwrap pouch in a carton (NDC 64950-381-14).

Store at 15°C to 25°C (59°F to 77°F). Discard used containers. Store unused containers in pouch to protect from light.

17 PATIENT COUNSELING INFORMATION

17.1 Directions for Use

Patients should be advised that ciprofloxacin otic solution, 0.2% is for otic use only. It is not for ophthalmic or inhalation use. It is not for injection.

Ciprofloxacin otic solution, 0.2% should be given 2 times each day (about 12 hours apart) in each infected ear.

Ciprofloxacin otic solution, 0.2% should be used for as long as it is prescribed, even if the symptoms improve. The patient should be advised to follow these directions while on

ciprofloxacin otic solution, 0.2%: Wash their hands before use.

Warm the container in their hands for at least one minute prior to use to minimize dizziness that may result from the instillation of a cold solution into the ear canal. Twist off and discard top of container.

Lie with the affected ear upward and then instill the contents of one container into the ear. Maintain this position for at least one minute to facilitate penetration of the drops into the ear.

- Repeat, if necessary, for the opposite ear.
- Discard used container.
- Store unused containers in pouch to protect from light.

17.2 Hypersensitivity

Patients should be advised to immediately discontinue ciprofloxacin otic solution, 0.2% at

the first appearance of a skin rash or any other sign of hypersensitivity [see Section 5.1 Warnings and Precautions].

Ciprofloxacin otic solution, 0.2% is Distributed by:
Genus Lifesciences Inc.
Allentown, PA 18102

PRINCIPAL DISPLAY PANEL - 14 Vial Carton

NDC 64950-381-14

Sterile
Preservative-Free

Ciprofloxacin Otic
Solution, 0.2%

Containers not for
individual sale.

Discard used containers.
Store at 15°C to 25°C (59°F to 77°F).
Store unused containers in pouch to
protect from light.

Contents: 14 single-dose containers,
0.25 mL each (deliverable volume)

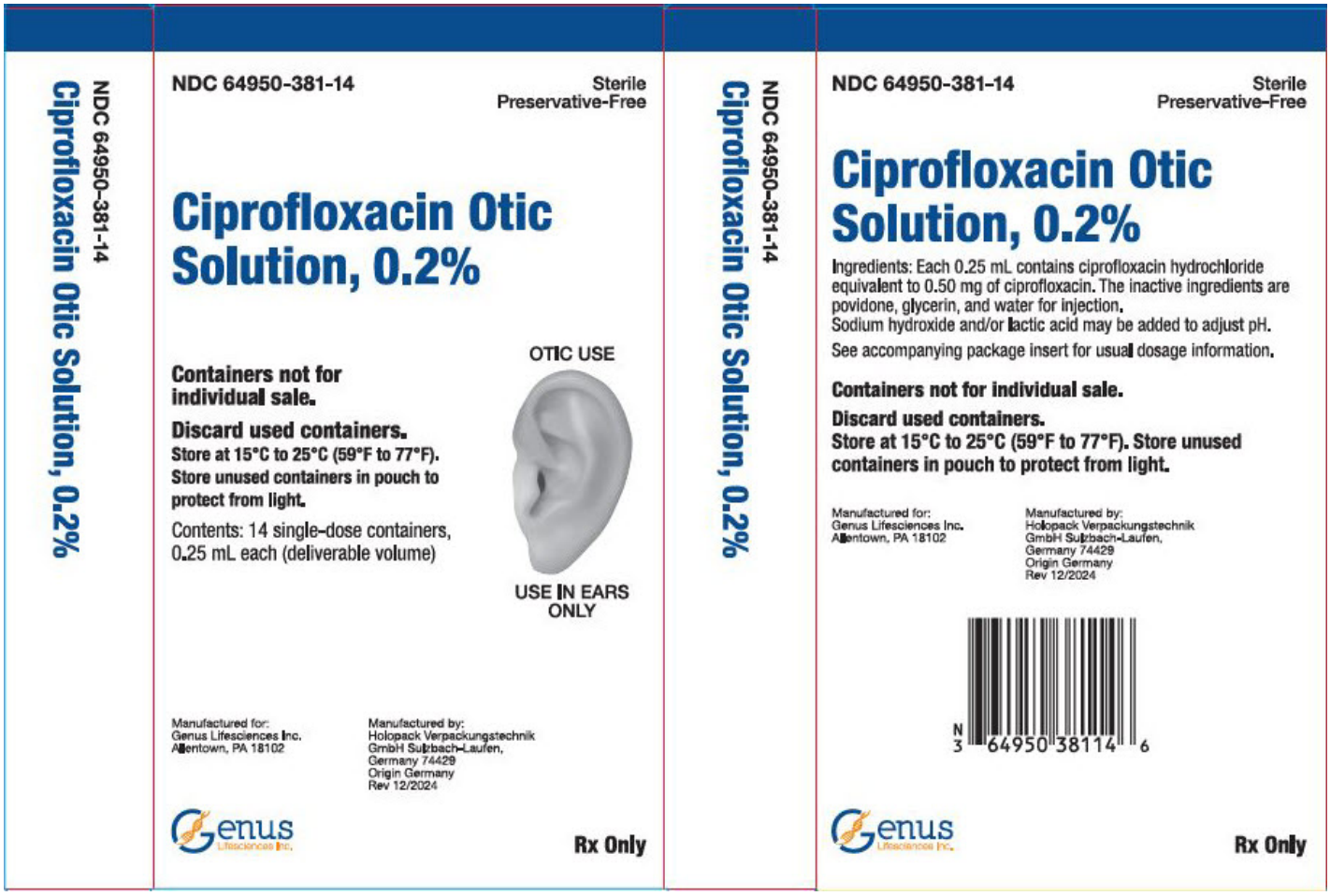
OTIC USE
USE IN EARS
ONLY

Manufactured for:
Genus Lifesciences Inc.
Allentown, PA 18102

Manufactured by:
Holopack Verpackungstechnik
GmbH Sulzbach-Laufen,
Germany 74429
Origin Germany
Rev 12/2024

Genus
Lifesciences Inc.

Rx Only



CIPROFLOXACIN OTIC

ciprofloxacin solution/ drops

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:64950-381
Route of Administration	AURICULAR (OTIC)		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Ciprofloxacin (UNII: 5E8K9I0O4U) (Ciprofloxacin - UNII:5E8K9I0O4U)	Ciprofloxacin	0.5 mg in 0.25 mL

Inactive Ingredients	
Ingredient Name	**Strength**
WATER (UNII: 059QF0KO0R)	
POVIDONE, UNSPECIFIED (UNII: FZ989GH94E)	
GLYCERIN (UNII: PDC6A3C0OX)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
LACTIC ACID, UNSPECIFIED FORM (UNII: 33X04XA5AT)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:64950-381-14	14 in 1 CARTON	12/01/2024	
1		0.25 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA217887	12/01/2024	

Labeler - Genus Lifesciences (113290444)

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