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

CETRAXAL (ciprofloxacin otic solution)
Initial U.S. Approval :1987

----------RECENT MAJOR CHANGES----------

Indications and Usage (1)	10/2026
Dosage and Administration (2)	10/2026
Contraindications (4)	10/2026
Warnings and Precautions (5)	10/2026

----------INDICATIONS AND USAGE----------
CETRAXAL is a fluoroquinolone antibacterial indicated for the treatment of acute otitis externa due to susceptible isolates of *Pseudomonas aeruginosa* or *Staphylococcus aureus*, in adults and pediatric patients one year of age and older. (1)

----------DOSAGE AND ADMINISTRATION----------
CETRAXAL is for otic administration only. It is not for ophthalmic use or injection.
Instill the contents of one single use container into the affected ear twice daily (approximately 12 hours apart) for 7 days. Use this dosing regimen for adults and pediatric patients aged one year or older. (2)

----------DOSAGE FORMS AND STRENGTHS----------
CETRAXAL 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 use container. (3)

----------CONTRAINDICATIONS----------
CETRAXAL is contraindicated in patients with a history of hypersensitivity to ciprofloxacin, other quinolones, or to any of the components of CETRAXAL. (4)

----------WARNINGS AND PRECAUTIONS----------
- Hypersensitivity: discontinue use at the first appearance of a skin rash or any other sign of hypersensitivity. (5.1)
- Growth of Resistant Organisms with Prolonged Use: Use of CETRAXAL may result in overgrowth of nonsusceptible organisms, including yeast and fungi. If such infections occur, discontinue use and institute alternative therapy. (5.2)

----------ADVERSE REACTIONS----------
The most common adverse reactions reported in 2-3% of patients receiving CETRAXAL were fungal ear superinfection, ear pruritus, headache and application site pain. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Ritedose Corporation at 1-803-935-4017or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 10/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

CETRAXAL is indicated for the treatment of acute otitis externa due to susceptible isolates of *Pseudomonas aeruginosa* or *Staphylococcus aureus,* in adults and pediatric patients one year of age and older.

2 DOSAGE AND ADMINISTRATION

CETRAXAL is for otic administration only. It is not for ophthalmic use or injection.

Instill the contents of one single use container (deliverable volume: 0.25 mL) into the affected ear twice daily (approximately 12 hours apart) for 7 days. Use this dosing regimen for adults and pediatric patients aged 1 year or older.

Wash hands before use. Warm the solution 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 instill the solution. Maintain this position for at least 1 minute to facilitate penetration of the drops into the ear. Repeat, if necessary, for the opposite ear *[see Instructions for Use]*.

3 DOSAGE FORMS AND STRENGTHS

CETRAXAL is a sterile, preservative-free, otic solution. Each single use container of CETRAXAL contains ciprofloxacin hydrochloride equivalent to 0.2 % ciprofloxacin (0.5 mg in 0.25 mL).

4 CONTRAINDICATIONS

CETRAXAL is contraindicated in patients with a history of hypersensitivity to ciprofloxacin, and to other quinolones, or any of the components of CETRAXAL.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity

CETRAXAL should be discontinued at the first appearance of a skin rash or any other sign of hypersensitivity.

5.2 Growth of Resistant Organisms with Prolonged Use

As with other anti-infectives, prolonged use of CETRAXAL may result in overgrowth of nonsusceptible organisms, including yeast and fungi. If such infections occur, discontinue use and institute alternative therapy.

5.3 Lack of Clinical Response

If the infection is not improved after one week of therapy, cultures can guide further treatment and evaluation.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Hypersensitivity *[see Warnings and Precautions (5.1)]*

6.1 Clinical Trials Experience

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.

Most Common Adverse Reactions

In a randomized, active-controlled clinical trial, approximately 319 patients with otitis externa were treated with CETRAXAL. The most common adverse reactions reported in approximately 2-3% of patients receiving CETRAXAL were fungal ear superinfection, ear pruritus, headache, and application site pain.

Other Adverse Reactions

Other adverse reactions occurring in less than 1% of patients treated were: tinnitus, dizziness and dermatitis.

6.2 Postmarketing Experience

No adverse reactions have been identified during post-approval use of CETRAXAL. The following adverse reactions have been identified during post approval use of topical fluroquinolones. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Skin and subcutaneous tissue disorders: generalized rash, toxic epidermolysis, dermatitis exfoliative, Stevens-Johnson syndrome, and urticaria.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Because of the minimal systemic absorption of ciprofloxacin following topical otic administration of CETRAXAL, this product is not expected to result in fetal exposure to the drug *[see Clinical Pharmacology (12.3)]*. There are no available data on CETRAXAL use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Additionally, prolonged experience with systemic administration of ciprofloxacin in pregnant women over several decades, based on available published information from case reports, case control studies and observational studies on ciprofloxacin administered during pregnancy, have not identified any drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes.

Animal reproduction studies have not been conducted with CETRAXAL. Oral administration of ciprofloxacin during organogenesis at doses up to 100 mg/kg to pregnant mice and rats, and intravenous administration at up to 30 mg/kg to pregnant rabbits did not cause fetal malformations *(see Data)*. These doses were at least 200 times the recommended otic human dose (ROHD) in mice, rats, and rabbits, based on body surface area (BSA).

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and of miscarriage is 15% to 20% respectively.

Data

Animal Data

Embryo-fetal developmental toxicology studies have been performed with ciprofloxacin in rats, mice, and rabbits. The doses used in these studies are, at a minimum, approximately 200 times greater than the recommended otic human dose based on body surface area, assuming total absorption of ciprofloxacin from the ear of a patient treated with CETRAXAL twice per day. In rats and mice, oral doses up to 100 mg/kg administered during organogenesis (Gestation Days (GD), 6 to 17) were not associated with adverse developmental outcomes, including embryo-fetal toxicity or malformations. In rabbits, oral administration of ciprofloxacin (30 and 100 mg/kg) produced

gastrointestinal disturbances resulting in maternal weight loss and an increased incidence of abortion, but no fetal malformations were observed at either dose. In rabbits, embryo-fetal toxicity, including increased incidence of abortion, can be associated with maternal toxicity due to disruption in the maternal microbiome. Intravenous administration of doses up to 20 mg/kg to pregnant rabbits was not maternally toxic and neither embryofetal toxicity nor fetal malformations were observed.

8.2 Lactation

Risk Summary

Because of the minimal systemic absorption of ciprofloxacin following topical otic administration of another ciprofloxacin otic product breastfeeding is not expected to result in the exposure of the infant to ciprofloxacin *[see Clinical Pharmacology (12.3)]*. It is not known whether ciprofloxacin is present in human milk following otic use. There is no data on the effects of ciprofloxacin on the breastfed infant or on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for CETRAXAL and any potential adverse effects on the breastfed child from CETRAXAL.

8.4 Pediatric Use

The safety and effectiveness of CETRAXAL for the treatment of acute otitis externa in pediatric patients one year of age and older have been established *[see Adverse Reactions (6.1) and Clinical Studies (14)]*.

The safety and effectiveness of CETRAXAL in pediatric patients below one year of age have not been established.

Animal Toxicity Data

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

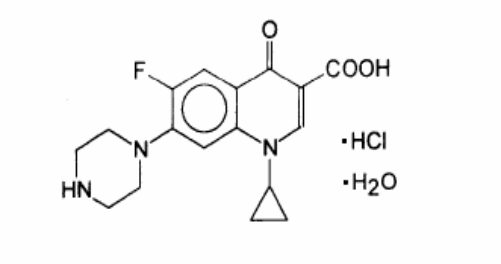
Clinical studies of CETRAXAL did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger adult patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

11 DESCRIPTION

CETRAXAL (ciprofloxacin otic solution) 0.2% contains synthetic ciprofloxacin hydrochloride, a fluoroquinolone antibacterial. CETRAXAL is a sterile, preservative-free solution for otic use. Each single use container of CETRAXAL delivers 0.25 mL of solution equivalent to 0.5 mg of ciprofloxacin (equivalent to 0.56 mg of ciprofloxacin hydrochloride). The inactive ingredients are povidone, glycerin, and water for injection. Sodium hydroxide and/or lactic acid may be added to adjust the pH to 4.5 - 5.0.

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 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 antibacterial *[see Microbiology (12.4)]*.

12.3 Pharmacokinetics

The plasma concentrations of ciprofloxacin were not measured following otic administration of 0.25 mL CETRAXAL (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

Mechanism of Action

The bactericidal action of ciprofloxacin results from inhibition of the enzymes topoisomerase II (DNA gyrase) and topoisomerase IV (both Type II topoisomerases), which are required for bacterial DNA replication, transcription, repair, and recombination.

Resistance

Bacterial resistance to quinolones can develop through chromosomally- or plasmid-

mediated mechanisms. Resistance to fluoroquinolones occurs primarily by either mutations in the DNA gyrases, decreased outer membrane permeability, or drug efflux. In vitro resistance to ciprofloxacin develops slowly by multiple step mutations. Resistance to ciprofloxacin due to spontaneous mutations occurs at a general frequency of between < 10^{-9} to $1x10^{-6}$.

In vitro studies demonstrated cross-resistance between ciprofloxacin and some fluoroquinolones. There is no known cross-resistance between ciprofloxacin and other classes of antibacterials.

Antimicrobial Activity

Ciprofloxacin has been shown to be active against most isolates of the following bacteria, both *in vitro* and in clinical infections *[see Indications and Usage (1)]*.

Gram-positive bacteria:

- *Staphylococcus aureus*

Gram-negative bacteria:

- *Pseudomonas aeruginosa*

13 NON-CLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

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 CETRAXAL have been performed to evaluate carcinogenic potential.

Mutagenesis

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).

Impairment of Fertility

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 200 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 CETRAXAL twice per day.

14 CLINICAL STUDIES

In a randomized, multi-center, evaluator-blinded study of 630 patients with acute otitis externa, 318 patients were treated with either CETRAXAL twice daily or 312 patients with neomycin and polymyxin B sulfates and hydrocortisone otic solution (PNH) three times daily for 7 days. The median age of patients enrolled in the clinical study was 14 years in the CETRAXAL group and 15 years in the PNH group, with about 50% of subjects less than 18 years of age. The primary efficacy endpoint was the proportion of patients with clinical cure at the test of cure visit (approximately 9 days after end of study treatment) in the per protocol population. Clinical cure was defined as the complete resolution of signs and symptoms of acute otitis externa (ear pain, edema, otorrhea) without the need for additional antimicrobial treatment.

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

16 HOW SUPPLIED/STORAGE AND HANDLING

CETRAXAL is a clear, colorless, sterile, preservative-free solution. CETRAXAL is supplied as a 0.2% otic solution in a low-density polyethylene (LDPE) single use container. Each single use container delivers 0.25 mL of solution equivalent to 0.5 mg of

ciprofloxacin; 14 single use containers are packaged in a foil overwrap pouch in a carton (NDC pending).

Store at 15ºC to 25ºC (59ºF to 77ºF). Discard used containers. Store unused containers in pouch to protect from light.

17 PATIENT COUNSELING INFORMATION

Advise the patient or caregiver to read the FDA-approved patient labeling (Instructions for Use).

Hypersensitivity

Advise patients to immediately discontinue CETRAXAL at the first appearance of a skin rash or any other sign of hypersensitivity *[see Warnings and Precautions (5.1)]*. Advise patients and/or their caregivers that if the ear continues to be painful, swollen or itchy after a week, they should consult their physician.

CETRAXAL is:

Manufactured by:
The Ritedose Corporation Columbia, SC 29203 USA

CETRAXAL® is a registered trademark of Laboratorios SALVAT, S.A.

INSTRUCTIONS FOR USE
CETRAXAL [SETRAK-sal]
(ciprofloxacin otic solution)

Read this Instructions for Use that come with CETRAXAL before you or your caregiver starts using it and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or treatment.

This Instructions for Use contain information on how to use CETRAXAL.
Important Information You Need to Know Before Using CETRAXAL:

- **CETRAXAL is for use in the ear only (otic use). Do not** use CETRAXAL in the eye or nose. **Do not** inject CETRAXAL**.**
- Use CETRAXAL exactly as your healthcare provider tells you to use it. Check with your healthcare provider or pharmacist if you are not sure.
- Each CETRAXAL container has enough medicine for one time use (single use).
- After you open the CETRAXAL container, use it right away and throw away (discard) after use.
- CETRAXAL liquid should be clear and colorless. **Do not** use if the liquid is cloudy or has color.
- Empty all of the CETRAXAL medicine from 1 single-use container into your affected ear. Do this **2 times a day,** about 12 hours apart for **7 days even if your symptoms improve before the 7 days**.
- **Do not** use CETRAXAL after the expiration date (EXP) printed on the outer carton, foil pouch and single use container.
  - The expiration date is the last day of the month shown. For example, 2026-DEC means the medicine expires December 31, 2026.

Preparing to Use CETRAXAL

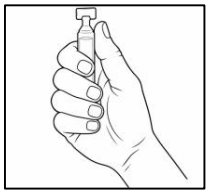
Follow these instructions each time you or your caregiver use CETRAXAL. Ask your healthcare provider if there is anything you or your caregiver do not understand.

Step 1. Wash your hands with soap and water.



Step 2. Remove the strip of single-use containers from the foil pouch. Break off 1 CETRAXAL single-use container from the strip.
Break off a second CETRAXAL container if you need to treat both ears. Place the remaining unopened CETRAXAL containers back into the foil pouch.

Step 3. Warm the CETRAXAL container by holding the container in your hand for at least 1 minute before use. Placing cold CETRAXAL liquid in your ear may cause dizziness.



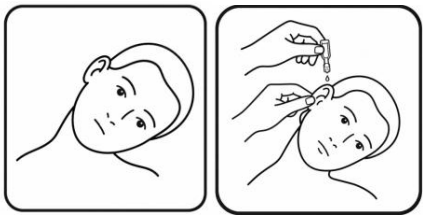
Using CETRAXAL

Step 4.

- Hold the CETRAXAL container upright. Make sure the medicine is in the bottom part of the single-use container.
- Twist off the top and throw it away.
- Do not touch the tip of the CETRAXAL container after removing the top.

Step 5.

- Lie down on your side with the affected ear facing up.
- Hold the CETRAXAL container between your thumb and pointer fingers.
- Squeeze one entire CETRAXAL container into the ear, releasing all the drops.
- Stay on your side with the affected ear facing up for at least 1 minute to allow CETRAXAL to enter the affected part of the ear.



Step 6. Throw away the used CETRAXAL container in your household trash.
Repeat Steps 3 through 6, if needed, to treat the opposite ear.

How should I store CETRAXAL?

- Store CETRAXAL container between 59°F to 77°F (15°C to 25°C).
- Store unopened CETRAXAL containers in the protective foil pouch they come in to protect from light.

Keep CETRAXAL and all medicines out of reach of children.

Manufactured by:
The Ritedose Corporation
Columbia, SC 29203 USA
Distributed by: Pending [name and place of business]

CETRAXAL® is a registered trademark of Laboratorios SALVAT, S.A.

This Instructions for Use has been approved by the U.S. Food and Drug Administration. Approved: October 2026