PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

Pr**CIPRODEX®**

Ciprofloxacin / Dexamethasone Otic Suspension
0.3% w/v (as ciprofloxacin hydrochloride) / 0.1% w/v

Antibacterial - Corticosteroid (Otic)

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Pr **CIPRODEX®**
Ciprofloxacin/Dexamethasone Otic Suspension

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Otic	Suspension/ 0.3% ciprofloxacin (as ciprofloxacin hydrochloride) and 0.1% dexamethasone	Benzalkonium chloride as preservative. *For a complete listing see Dosage Forms, Composition and Packaging section.*

INDICATIONS AND CLINICAL USE

CIPRODEX® (ciprofloxacin/dexamethasone otic suspension) is indicated for the treatment of infections caused by most strains of the designated microorganisms in the specific conditions listed below:

Acute Otitis Media with Otorrhea through tympanostomy tubes in pediatric patients ≥ 6 months of age due to:
Aerobic, Gram-Positive:
Streptococcus pneumoniae
Staphylococcus aureus

Aerobic, Gram-Negative:
Haemophilus influenza
Moraxella catarrhalis
Pseudomonas aeruginosa

Acute Otitis Externa in adults and pediatric patients ≥ 1 year of age due to:
Aerobic, Gram-Positive:
Staphylococcus aureus

Aerobic, Gram-Negative:
Pseudomonas aeruginosa

To reduce the development of drug-resistant bacteria and maintain the effectiveness of CIPRODEX and other antibacterial drugs, CIPRODEX should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria.

Geriatrics (> 65 years of age): Elderly patients may be at a higher risk of developing tendon

inflammation and rupture (see **WARNINGS AND PRECAUTIONS, General**).

Pediatrics (< 6 months of age): The safety and effectiveness of CIPRODEX have not been evaluated in pediatric patients < 6 months of age.

CONTRAINDICATIONS

CIPRODEX is contraindicated in patients with:

- Hypersensitivity to ciprofloxacin, dexamethasone or to any ingredient in the formulation or component of the container. For a complete listing, see *Dosage Forms, Composition and Packaging* section.
- Hypersensitivity to other quinolones, including nalidixic acid.
- Hypersensitivity to other corticosteroids.
- Viral infections of the external canal, including herpes simplex infections.
- Fungal otic infections.
- Parasitic otic infections.

WARNINGS AND PRECAUTIONS

FOR TOPICAL OTIC USE ONLY.

NOT FOR OPHTHALMIC USE.

NOT FOR INJECTION.

General

CIPRODEX 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. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial edema), airway obstruction, dyspnea, urticarial and itching. Serious acute hypersensitivity reactions may require immediate emergency treatment. Oxygen and airway management should be administered as clinically indicated.

Corticosteroids may reduce resistance to and aid in the establishment of non-susceptible bacterial, fungal, parasitic or viral infections and mask the clinical signs of infection.

If the infection is not improved after one week of treatment, alternate therapy should be considered.

If otorrhea persists after a full course of therapy, or if 2 or more episodes of otorrhea occur within 6 months, further evaluation is recommended to exclude an underlying condition, such as cholesteatoma, foreign body, or a tumor.

The systemic administration of quinolones, including ciprofloxacin at doses much higher than given or absorbed by the otic route, has led to lesions or erosions of the cartilage in weight-bearing joints and other signs of arthropathy in immature animals of various species.

Tendon inflammation and rupture may occur with systemic fluoroquinolone therapy, including ciprofloxacin, particularly in elderly patients and in those treated concurrently with corticosteroids. Therefore, treatment with CIPRODEX should be discontinued at the first sign of tendon inflammation.

Spontaneous extrusion of tympanostomy tubes is not unexpected and occurred at an incidence of 1.8% in the CIPRODEX treatment group in the clinical trials.

CIPRODEX contains the preservative benzalkonium chloride, which may be an irritant and cause skin reactions.

Sexual Function/Reproduction

Studies have not been performed to evaluate the effect of topical administration of the combination of ciprofloxacin and dexamethasone on human fertility. Topical dermal studies in animals have shown effects on male sex organs following long-term use of dexamethasone at high doses (see **TOXICOLOGY, Reproduction & Teratology**).

Special Populations

Pregnant Women: 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 20mg/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. The teratogenic potential of dexamethasone after topical (ophthalmic) treatment has been investigated in New Zealand white rabbits. Treatment with a 0.1% suspension of dexamethasone into the conjunctival sac on days 6 through 18 of gestation resulted in a 15.6% and 32.3% incidence of fetal anomalies in two groups of rabbits.

Animal reproduction studies have not been conducted with CIPRODEX. No adequate and well controlled studies have been performed in pregnant women. Prolonged or repeated systemic corticoid use during pregnancy has been associated with an increased risk of intra-uterine growth retardation. Infants born of mothers who received substantial doses of corticosteroids during pregnancy should be observed carefully for signs of hypoadrenalism. Caution should be exercised when CIPRODEX is used by a pregnant woman.

Nursing Women: Ciprofloxacin and corticosteroids, as a class, appear in milk following oral

administration. Dexamethasone in breast milk could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical otic administration of ciprofloxacin or dexamethasone could result in sufficient systemic absorption to produce detectable quantities in human milk. Because of the potential for unwanted effects 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 and the low dose used in topical otic therapy.

Pediatrics (< 6 months of age): The safety and effectiveness of CIPRODEX have not been established in pediatric patients < 6 months of age.

Pediatrics (≥ 6 months of age): The safety and efficacy of CIPRODEX have been established in pediatric patients 6 months and older (937 patients) in clinical trials.

No clinically relevant changes in hearing function were observed in 69 pediatric patients (age 4 to 12 years) treated with CIPRODEX and tested for audiometric parameters.

Although ciprofloxacin and other quinolones cause arthropathy in immature animals after oral administration, topical ocular administration of ciprofloxacin to immature dogs did not cause any arthropathy and there is no evidence that the otic dosage form has any effect on the weight bearing joints.

Susceptibility/Resistance

Development of Drug-Resistant Bacteria: Prescribing CIPRODEX in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and risks the development of resistant drug-resistant bacteria.

Potential for Microbial Overgrowth: As with other antibacterial preparations, prolonged use of CIPRODEX may result in overgrowth of non-susceptible organisms, including yeast and fungi. If superinfection occurs, discontinue use and institute alternative therapy.

ADVERSE REACTIONS

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

In Phase II and III clinical trials, a total of 937 patients were treated with CIPRODEX. This included 400 patients with acute otitis media with otorrhea and 537 patients with acute otitis externa. The reported treatment-related adverse events are listed below:

Acute Otitis Media in pediatric patients with tympanostomy tubes

The following treatment-related adverse events occurred in 0.5% or more of the patients with non-intact tympanic membranes.

Adverse Event	Incidence (N=400)
Ear discomfort	3.0%
Ear pain	2.3%
Ear precipitate (residue)	0.5%
Irritability	0.5%
Taste perversion	0.5%

The following treatment-related adverse events were each reported in a single patient: tympanostomy tube blockage; ear pruritus; tinnitus; candidiasis; crying; dizziness; and erythema.

Acute Otitis Externa

The following treatment-related adverse events occurred in 0.4% or more of the patients with intact tympanic membranes.

Adverse Event	Incidence (N=537)
Ear pruritus	1.5%
Ear debris	0.6%
Superimposed ear infection	0.6%
Ear congestion	0.4%
Ear pain	0.4%
Erythema	0.4%

The following treatment-related adverse events were each reported in a single patient: ear discomfort; decreased hearing; and ear disorder (tingling).

Post-Market Adverse Drug Reactions

Adverse reactions identified from subsequent clinical trials are listed below.
Ear and labyrinth disorders: ear infection fungal, otorrhea;
Gastrointestinal disorders: vomiting;
General disorders and administration site conditions: device occlusion;
Nervous system disorders: headache;
Skin and subcutaneous tissue disorders: skin exfoliation.

Adverse reactions identified via spontaneous reporting are listed below.
Ear and labyrinth disorders: auricular swelling;
Immune system disorders: hypersensitivity.

DRUG INTERACTIONS

Specific drug interaction studies have not been conducted with CIPRODEX administered in the ear.

DOSAGE AND ADMINISTRATION

Recommended Dose

Acute Otitis Media in pediatric patients (≥ 6 months of age) with tympanostomy tubes:
Four drops instilled into the affected ear twice daily for seven days.

Acute Otitis Externa in adult patients and pediatric patients (≥ 1 year of age):
Four drops instilled into the affected ear twice daily for seven days.

Missed Dose

If a dose is missed, it should be given as soon as possible. If it is almost time for the next dose, skip the missed dose and go back to the regular dosing schedule.

Administration

SHAKE WELL IMMEDIATELY BEFORE USING.

Acute Otitis Media in pediatric patients (≥ 6 months of age) with tympanostomy tubes:
The suspension should be warmed by holding the bottle in the hand for one or two minutes to avoid dizziness, which may result from the instillation of a cold suspension. The patient should lie with the affected ear upward, and then the drops should be instilled. The tragus should then be pumped 5 times by pushing inward to facilitate penetration of the drops into the middle ear. This position should be maintained for 60 seconds. Repeat, if necessary, for the opposite ear. Discard unused portion after therapy is completed.

Acute Otitis Externa in adult patients and pediatric patients (≥ 1 year of age):
The suspension should be warmed by holding the bottle in the hand for one or two minutes to avoid dizziness, which may result from the instillation of a cold suspension. The patient should lie with the affected ear upward, and then the drops should be instilled. This position should be maintained for 60 seconds to facilitate penetration of the drops into the ear canal. Repeat, if necessary, for the opposite ear. Discard unused portion after therapy is completed.

OVERDOSAGE

There is no known treatment of overdosage since overdosage in the use of topical otic preparations is a remote possibility. Discontinue medication when heavy or protracted use is suspected.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Ciprofloxacin, a fluoroquinolone antibiotic, has *in vitro* activity against a wide range of gram-positive and gram-negative microorganisms. The bactericidal action of ciprofloxacin results from inhibition of the enzyme, DNA gyrase, which is required for the synthesis of bacterial DNA.

Dexamethasone, a potent corticosteroid, has been shown to aid in the resolution of inflammation.

Pharmacokinetics

Following a single bilateral 4-drop topical otic dose of CIPRODEX to pediatric patients following tympanostomy tube insertion, measurable plasma concentrations of ciprofloxacin and dexamethasone were observed up to 6 hours. In 25 patients, the mean (± SD) peak plasma concentrations of ciprofloxacin and dexamethasone were 1.14 ± 0.98 ng/mL and 0.86 ± 1.19 ng/mL, respectively, and were observed typically within 15 minutes to 2 hours post-dose. For ciprofloxacin, these levels were approximately 650-fold lower than levels achieved with an oral dose of 250 to 1000 mg.[1] This bilateral exposure resulted in a peak dexamethasone concentration approximately 9-fold lower than reported by following an oral 0.5mg dose.[2] Estimates of half-life averaged 3.1 hours for ciprofloxacin and 4.5 hours for dexamethasone. Both values are similar to those reported after oral doses in adults.[1,3] While systemic exposure was assessed with bilateral administration, most AOMT patients in the clinical trials for this product had unilateral infections (77%).

STORAGE AND STABILITY

Store at room temperature (15°C to 30° C). Avoid freezing. Protect from light. Keep out of reach and sight of children.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Each mL of CIPRODEX contains:
Medicinal Ingredients: Ciprofloxacin Hydrochloride (equivalent to 3 mg ciprofloxacin base) and 1 mg Dexamethasone.
Preservative: 0.1 mg benzalkonium chloride.
Non-medicinal Ingredients: boric acid, sodium chloride, hydroxyethyl cellulose, tyloxapol, acetic acid, sodium acetate, edetate disodium and purified water. Sodium hydroxide and/or hydrochloric acid may be added for adjustment of pH.

CIPRODEX has a pH of approximately 5 and an osmolality of approximately300 mOsm/kg.

CIPRODEX is supplied as follows: 7.5 mL fill in a natural polyethylene bottle and natural plug, with a white polypropylene closure. Tamper evidence is provided with a shrink band around the

closure and neck area of the package.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

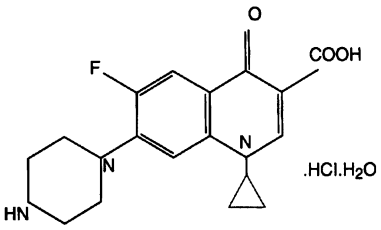
Drug Substance

Proper name: Ciprofloxacin Hydrochloride

Chemical name: 1 cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid, hydrochloride monohydrate

Molecular formula and molecular mass: $C_{17}H_{18}FN_30_3 \cdot HCl \cdot H_20$; 385.8

Structural formula:



Physicochemical properties: Ciprofloxacin is a faintly yellowish to light yellow crystalline substance. Ciprofloxacin is readily water soluble and the pH of a 2.5% solution is about 4.

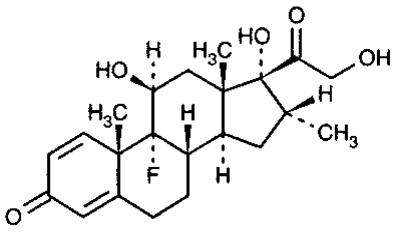
Drug Substance

Proper name: Dexamethasone

Chemical name: 9-Fluoro-11β,17,21-trihydroxy-16∀-methylpregna-1,4-diene-3,20-dione

Molecular formula and molecular mass: $C_{22}H_{29}FO_5$; 392.47

Structural formula:



Physicochemical properties: Dexamethasone is a white to practically white crystalline powder, and is practically insoluble in water, sparingly soluble in alcohol, and slightly soluble in chloroform. The melting point is about 250°C with decomposition.

CLINICAL TRIALS

In a randomized, multicenter, controlled clinical trial, CIPRODEX® dosed 2 times per day for 7 days demonstrated clinical cures in the per protocol analysis in 86% of AOMT patients compared to 79% for ofloxacin solution, 0.3%, dosed 2 times per day for 10 days. Among culture positive patients, clinical cures were 90% for CIPRODEX compared to 79% for ofloxacin solution, 0.3%. Microbiological eradication rates for these patients in the same clinical trial were 91% for CIPRODEX compared to 82% for ofloxacin solution, 0.3%.

In 2 randomized multicenter, controlled clinical trials, CIPRODEX dosed 2 times per day for 7 days demonstrated clinical cures in 87% and 94% of per protocol evaluable AOE patients, respectively, compared to 84% and 89%, respectively, for otic suspension containing neomycin 0.35%, polymyxin B 10,000 IU/mL, and hydrocortisone 1.0% (neo/poly/HC). Among culture positive patients clinical cures were 86% and 92% for CIPRODEX compared to 84% and 89%, respectively, for neo/poly/HC. Microbiological eradication rates for these patients in the same clinical trials were 86% and 92% for CIPRODEX compared to 85% and 85%, respectively, for neo/poly/HC.

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.

The following table shows the *in vitro* activity of ciprofloxacin.

Acute Otitis Media with Otorrhea

Pathogen	N	MIC range µg/mL	MIC_{50} µg/mL	MIC_{90} µg/mL
Aerobic, Gram-Positive				
Staphylococcus aureus	54	0.13 - 16	0.25	1.0
Streptococcus pneumoniae	48	0.25 - 4.0	1.0	2.0
Aerobic, Gram-Negative				
Haemophilus influenzae	36	0.004 - 0.13	0.008	0.016
Moraxella catarrhalis	11	0.013 - 0.06	0.03	0.06
Pseudomonas aeruginosa	48	0.06 - 2.0	0.25	0.50

Acute Otitis Externa

Pathogen	N	MIC range µg/mL	MIC_{50} µg/mL	MIC_{90} µg/mL
Aerobic, Gram-Positive				
Staphylococcus aureus	41	0.13 - 2.0	0.25	1.0
Staphylococcus haemolyticus	13	0.13 - 16	0.25	16
Enterococcus faecalis	29	0.50 - 2.0	1.0	2.0
Aerobic, Gram-Negative				
Acinetobacter genospecies 3	15	0.06 - 4.0	0.13	4.0
Enterobacter aerogenes	20	0.008 - 0.13	0.016	0.03
Enterobacter cloacae	12	0.004 - 0.03	0.016	0.03
Klebsiella pneumoniae	18	0.016 - 0.06	0.03	0.06
Proteus mirabilis	10	0.016 - 0.03	0.03	0.03
Pseudomonas aeruginosa	235	0.016-1.0	0.13	0.25
Pseudomonas stutzeri	10	0.016 - 0.25	0.13	0.25
Serratia marcescens	15	0.03 - 1.0	0.06	0.50

Resistance:
Cross-resistance has been observed between ciprofloxacin and other fluoroquinolones. There is generally no cross-resistance between quinolones and other classes of antibacterial agents such as β-lactams or aminoglycosides.

TOXICOLOGY

Single-Dose Toxicity
The single-dose toxicity of ciprofloxacin has been established in several species. The oral LD_{50} in rats and mice is > 5000 mg/kg, and about 2500 mg/kg in rabbits. Emesis in dogs and cats precluded determination of oral LD_{50}s in these species. However, in cats it was shown to be greater than 150 mg/kg. The intramuscular LD_{50} was >1000 mg/kg in rats and mice.

Several routes of administration have been used to determine the single-dose toxicity of dexamethasone. The oral LD_{50} of dexamethasone in rats is > 3000 mg/kg. Subcutaneous LD_{50}s are 14 mg/kg, 4400 mg/kg and 7200 µg/kg in rats, mice and rabbits, respectively. Intraperitoneal LD_{50}s are 54 mg/kg in rats and 410 mg/kg in mice.

The single dose exposure to ciprofloxacin and dexamethasone from the instillation of four drops of the CIPRODEX into the affected ear is 0.42 mg ciprofloxacin and 0.14 mg dexamethasone. Administration of this product to a 10 kg child twice daily in both ears would result in exposures of 0.168 mg/kg ciprofloxacin and 0.056 mg/kg dexamethasone. These doses are >800 and >50,000 fold lower than the lowest oral LD_{50}s reported for ciprofloxacin and dexamethasone, respectively. In the event that a 10 kg child should accidentally ingest the entire contents of a 7.5 ml vial of CIPRODEX they would receive a dose of 2.25 mg/kg ciprofloxacin and 0.75 mg/kg

dexamethasone. These doses are 66 and 4,000 fold lower that the lowest oral LD_{50}s for ciprofloxacin and dexamethasone respectively.

Mutagenicity:
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 V $_{79}$ 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)

Carcinogenicity:
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 CIPRODEX have been performed to evaluate carcinogenic potential.

Long term studies have not been performed to evaluate the carcinogenic potential of topical otic dexamethasone. Dexamethasone has been tested for *in vitro* and *in vivo* genotoxic potential and shown to be positive in the following assays; chromosomal aberrations, sister-chromatid exchange in human lymphocytes and micronuclei and sister-chromatid exchanges in mouse bone marrow. However, the Ames/Salmonella assay, both with and without S9 mix, did not show any increase in His^+ revertants.

Reproduction & Teratology:
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, assuming total absorption of ciprofloxacin from the ear of a 10kg child treated with CIPRODEX twice per day according to label directions.

The effect of dexamethasone on fertility has not been investigated following topical otic application. However, the lowest toxic dose of dexamethasone identified following topical dermal application was 1802 µg/kg in a 26-week study in male rats and resulted in changes to the testes, epididymis, sperm duct, prostate, seminal vesicle, Cowper's gland and accessory glands. The relevance of this study for topical otic use is unknown; however this dose is > 150 fold

higher than the exposure which would occur if a 50 kg adult used CIPRODEX in both ears twice a day as indicated.

Local Tolerance Studies:
Guinea pigs dosed in the middle ear with CIPRODEX for one month exhibited no drug-related structural or functional changes of the cochlear hair cells and no lesions in the ossicles. CIPRODEX was also shown to lack dermal sensitizing potential in the guinea pig when tested according to the method of Buehler.

REFERENCES

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READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

CIPRODEX®
Ciprofloxacin/Dexamethasone Otic Suspension

Read this carefully before you start taking **CIPRODEX®** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **CIPRODEX**.

What is CIPRODEX used for?
CIPRODEX is used to treat:

- **Middle Ear Infections with Drainage through a Tube in Patients 6 months and older.** A middle ear infection is a bacterial infection behind the eardrum. People with a tube in the eardrum may notice drainage from the ear canal.
- **Outer Ear Canal Infection in Patients 1 year and older.** An outer ear canal infection, also known as "swimmer's ear," is a bacterial infection of the outer ear canal. The ear canal and outer part of the ear may swell, turn red and be painful. A fluid discharge may also appear in the ear canal.

Antibacterial drugs like CIPRODEX treat only bacterial infections. They do not treat viral infections. Although you may feel better early in your treatment, CIPRODEX should be used exactly as directed. Misuse or overuse of CIPRODEX could lead to the growth of bacteria that will not be killed by CIPRODEX (resistance). This means that CIPRODEX may not work for you in the future. Do not share your medicine.

How does CIPRODEX work?
CIPRODEX contains two medicinal ingredients. Ciprofloxacin, an antibiotic, kills bacteria. Dexamethasone, a steroid, reduces inflammation.

What are the ingredients in CIPRODEX?
Medicinal ingredients: ciprofloxacin hydrochloride and dexamethasone.
Non-medicinal ingredients: acetic acid, benzalkonium chloride (as preservative), boric acid, edetate disodium, hydroxyethyl cellulose, sodium acetate, sodium chloride, sodium hydroxide and/or hydrochloric acid (to adjust pH), tyloxapol, and purified water.

CIPRODEX comes in the following dosage forms:
Ear drops, 0.3% w/v ciprofloxacin (as ciprofloxacin hydrochloride) and 0.1% w/v dexamethasone

Do not use CIPRODEX if:

- You or your child is allergic to ciprofloxacin, dexamethasone or any other of the ingredients in CIPRODEX (see **What are the ingredients in CIPRODEX?**).
- You or your child is allergic to other quinolone antibiotics, including nalidixic acid.

- You or your child is allergic to other steroids.
- You or your child has a viral infection of the outer ear canal, including herpes simplex (often called a cold sore).
- You or your child has a fungal ear infection.
- You or your child has a parasitic ear infection.
- Your child is under 6 months old.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take CIPRODEX. Talk about any health conditions or problems you may have, including if you:

- Have a skin rash or any other allergic reaction, including hives, itching or breathing problems. You should stop treatment and immediately contact your healthcare professional. You may need emergency treatment.
- Notice your symptoms get worse or suddenly return. You should contact your healthcare professional. You may become more susceptible to infections especially after prolonged use.
- Feel pain, swelling or inflammation of the tendons while, or soon after taking CIPRODEX. You should stop treatment and contact your healthcare professional.
- If you develop another infection, your healthcare professional will prescribe another medicine to treat that infection.
- Are taking another steroid. You may be at a higher risk for developing tendon inflammation.
- Are pregnant or planning to become pregnant. The use of CIPRODEX is not recommended during pregnancy.
- Are breastfeeding or planning to breastfeed. The use of CIPRODEX is not recommended during breastfeeding.

Other warnings you should know about:
Only use CIPRODEX in your ear(s).

It is important that you keep your infected ear(s) clean and dry. Avoid getting the infected ear(s) wet. Avoid swimming unless your healthcare professional tells you it is okay.
If the infection is not improved after one week, you should consult your healthcare professional. If you have two or more episodes of drainage within six months, it is recommended you see your healthcare professional for further testing.

The preservative in CIPRODEX, benzalkonium chloride, may irritate your skin.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take CIPRODEX?

1. **Wash hands.** The person giving CIPRODEX should wash his/her hands.

2. **Warm and shake bottle.** Warm the CIPRODEX bottle in the hands for 1 to 2 minutes,

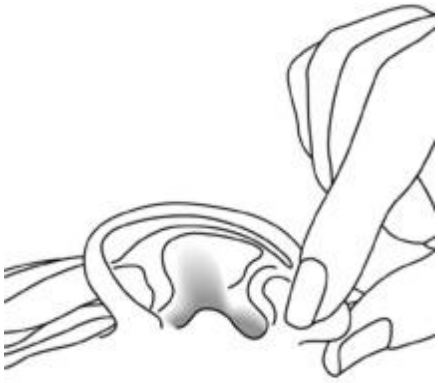
and then shake well.

3. **Add drops.** The person receiving CIPRODEX should lie on his/her side with the infected ear facing up. Apply 4 drops into the infected ear(s). To avoid contamination, do not let the tip of the bottle touch the fingers, ear or any other surfaces.

4. **BE SURE TO FOLLOW THE INSTRUCTIONS BELOW FOR THE SPECIFIC TYPE OF EAR INFECTION.**

   Middle Ear Infection with Tubes: While the person receiving CIPRODEX lies on his/her side, the person giving the drops should gently press the tragus (see image below) 5 times in a pumping motion after the drops have been given. This allows the drops to pass through the tube and into the middle ear.

   Outer Ear Infection: While the person receiving the drops lies on his/her side, the person giving the drops should gently pull the outer ear lobe upward and backward after the drops have been given (see image below). This allows the drops to flow down into the ear canal.



5. **Stay on side.** The person receiving CIPRODEX should remain on his/her side for at least 1 minute.

6. **Repeat steps 2-5 if both ears are infected.**

Usual dose:
4 drops in the infected ear(s), 2 times a day (about 12 hours apart) for 1 week or as long as your healthcare professional has told you. It is very important to use the ear drops as long as your healthcare professional has told you even if your ear infection gets better.

Overdose:

If you accidentally ingest CIPRODEX or think you have taken too much CIPRODEX, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

If a drop misses your ear, try again.

If you forget to apply a dose of CIPRODEX, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose and go back to the regular schedule. Do not use a double dose unless the healthcare professional has instructed you to do so.

What are possible side effects from using CIPRODEX?

These are not all the possible side effects you may feel when taking CIPRODEX. If you experience any side effects not listed here, contact your healthcare professional.

Middle Ear Infections: The most common side effect is ear discomfort or pain. Other side effects include: white, flaking, scaling material in the ear, irritability and abnormal taste in the mouth.
Outer Ear Canal Infections: The most common side effect is itching of the ear. Other side effects include: flaking, scaling material in the ear, fungal infection of the treated ear, feeling of fullness of plugging in the ear, ear pain and skin rash.
Other side effects include discharge from the ear, vomiting, headache, skin peeling and swelling of the ear.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
UNKNOWN Allergic reaction: swelling of face, lips of tongue; difficulty breathing; hives; itchy skin			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects
You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Store at room temperature (15°C to 30° C). Avoid freezing. Store the bottle in the carton.

Keep out of reach and sight of children.

If you want more information about CIPRODEX:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada.html); the manufacturer's website www.novartis.ca or by calling 1-800-363-8883.

This leaflet was prepared by Novartis Pharmaceuticals Canada Inc.

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