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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 (stinging).

DOSAGE AND ADMINISTRATION

CIPRODEX® OTIC SHOULD BE SHAKEN WELL IMMEDIATELY BEFORE USE

CIPRODEX® Otic contains 3 mg/mL (3000 µg/mL) ciprofloxacin and 1 mg/mL dexamethasone.

Acute Otitis Media in pediatric patients with tympanostomy tubes: The recommended dosage regimen for the treatment of acute otitis media in pediatric patients (age 6 months and older) through tympanostomy tubes is:

Four drops (0.14 mL, 0.42 mg ciprofloxacin, 0.14 mg dexamethasone) instilled into the affected ear twice daily for seven days. 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: The recommended dosage regimen for the treatment of acute otitis externa is: For patients (age 6 months and older): Four drops (0.14 mL, 0.42 mg ciprofloxacin, 0.14 mg dexamethasone) instilled into the affected ear twice daily for seven days. 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.

HOW SUPPLIED

CIPRODEX® (ciprofloxacin 0.3% and dexamethasone 0.1%) Sterile Otic Suspension is supplied as follows: 7.5 mL fill in a DROP-TAINER® system. The DROP-TAINER® system consists of 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.

NDC 0065-8533-02, 7.5 mL fill

Storage:

Store at controlled room temperature, 15°C to 30°C (59°F to 86°F). Avoid freezing. Protect from light.

CLINICAL STUDIES

In a randomized, multicenter, controlled clinical trial, CIPRODEX® Otic 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® Otic compared to 79% for ofloxacin solution, 0.3%. Microbiological eradication rates for these patients in the same clinical trial were 91% for CIPRODEX® Otic compared to 82% for ofloxacin solution, 0.3%. In 2 randomized multicenter, controlled clinical trials, CIPRODEX® Otic 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® Otic 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® Otic compared to 85% and 85%, respectively, for neo/poly/HC.

REFERENCES

1. Campoli-Richards DM, Monk JP, Price A, Benfield P, Todd PA, Ward A. Ciprofloxacin: A review of its antibacterial activity, pharmacokinetic properties and therapeutic use. *Drugs* 1988;35:373-447.

PATIENT INFORMATION

CIPRODEX® (CIPRODEX)

(ciprofloxacin 0.3% and dexamethasone 0.1%)

Sterile Otic Suspension

IMPORTANT PATIENT INFORMATION AND INSTRUCTIONS. READ BEFORE USE.

What is CIPRODEX® Otic?

CIPRODEX® Otic is an antibiotic/steroid combination product in a sterile suspension used to treat:

- **Middle Ear Infection with Drainage Through a Tube in Children 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 6 months 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 the outer part of the ear may swell, turn red, and be painful. Also, a fluid discharge may appear in the ear canal.

Who should NOT use CIPRODEX® Otic?

- Do not use this product if allergic to ciprofloxacin or to other quinolone antibiotics.
- Do not use this product if allergic to dexamethasone or to other steroids.
- Do not give this product to pediatric patients who are less than 6 months old.

How often should CIPRODEX® Otic be given?

CIPRODEX® Otic ear drops should be given 2 times each day (about 12 hours apart, for example, 8 AM and 8 PM) in each infected ear unless the doctor has instructed otherwise. The best times to use the ear drops are in the morning and at night. It is very important to use the ear drops for as long as the doctor has instructed, even if the symptoms improve. If CIPRODEX® Otic ear drops are not used for as long as the doctor has instructed, the infection may return.

What if a dose is missed?

If a dose of CIPRODEX® Otic 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. Do not use a double dose unless the doctor has instructed you to do so. If the infection is not improved after one week, you should consult your doctor. If you have two or more episodes of drainage within six months, it is recommended you see your doctor for further evaluation.

What activities should be avoided while using CIPRODEX® Otic?

It is important that the infected ear(s) remain clean and dry. When bathing, avoid getting the infected ear(s) wet. Avoid swimming unless the doctor has instructed otherwise.

What are the possible side effects of CIPRODEX® Otic?

During the testing of CIPRODEX® Otic for middle ear infections, the most common side effect related to CIPRODEX® Otic was ear discomfort that occurred in up to 3 out of 100 patients. Other common side effects were: ear pain; ear precipitate (residue); irritability; and abnormal taste. During the testing of CIPRODEX® Otic for ear canal infections, the most common side effect related to CIPRODEX® Otic was itching of the ear that occurred in 1 to 2 out of 100 patients. Other common side effects were: ear debris; ear infection in the treated ear; ear congestion; ear pain; and rash.

If any of these side effects persist, call the doctor.

If an allergic reaction to CIPRODEX® Otic occurs, stop using the product and contact your doctor.

DO NOT TAKE BY MOUTH

If CIPRODEX® Otic is accidentally swallowed or overdose occurs, call the doctor immediately. This medicine is available only with a doctor's prescription. Use only as directed. Do not use this medicine if outdated. If you wish to learn more about CIPRODEX® Otic, call your doctor or pharmacist.

HOW SUPPLIED

CIPRODEX® Otic is supplied as follows: 7.5 mL fill in a DROP-TAINER® system. The DROP-TAINER® system consists of 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.

NDC 0065-8533-02, 7.5 mL fill

Storage:

Store at controlled room temperature, 15°C to 30°C (59°F to 86°F). Avoid freezing. Protect from light.

U.S. Patent Nos. 4,844,902; 6,284,804; 6,359,016

CIPRODEX® is a registered trademark of Bayer AG.

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Manufactured by Alcon Laboratories, Inc.

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2. Warm & shake bottle

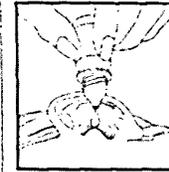


Hold the bottle of CIPRODEX® Otic in the hand for one or two minutes to warm the suspension, then shake well.

3. Add drops



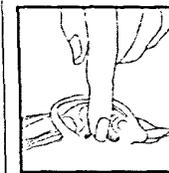
The person receiving CIPRODEX® Otic should lie on his/her side with the infected ear up.



Patients should have 4 drops of CIPRODEX® Otic put into the infected ear. The tip of the bottle should not touch the fingers or the ear or any other surfaces.

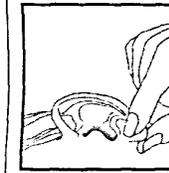
BE SURE TO FOLLOW INSTRUCTIONS BELOW FOR THE PATIENT'S SPECIFIC EAR INFECTION.

4. For Patients with Middle Ear Infection with Tubes:



While the person receiving CIPRODEX® Otic lies on his/her side, the person giving the drops should gently press the tragus (see diagram) 5 times in a pumping motion. This will allow the drops to pass through the tube in the eardrum and into the middle ear.

5. For Patients with Outer Ear Infection ("Swimmer's Ear"):



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. This will allow the ear drops to flow down into the ear canal.

6. Stay on side



The person who received the ear drops should remain on his/her side for at least 60 seconds. Repeat Steps 2-5 for the other ear if both ears are infected.

PATADAY™

(olopatadine hydrochloride ophthalmic solution) 0.2%

DESCRIPTION

PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% is a sterile ophthalmic solution containing olopatadine for topical administration to the eyes. Olopatadine hydrochloride is a white, crystalline, water-soluble powder with a molecular weight of 373.88 and a molecular formula of C₂₁H₂₃N₃ • HCl. The chemical structure is presented below:

Chemical Name: 111-[(Z)-3-(Dimethylamino) propylidene]-6-11-dihydroindenz[b,e] oxepin-2-acetic acid, hydrochloride.

Each mL of PATADAY™ solution contains: **Active:** 2.22 mg olopatadine hydrochloride equivalent to 2 mg olopatadine. **Inactives:** povidone; dibasic sodium phosphate; sodium chloride; edetate disodium; benzalkonium chloride 0.01% (preservative) hydrochloric acid / sodium hydroxide (adjust pH); and purified water.

Information will be superseded by supplements and subsequent editions

It has a pH of approximately 7 and an osmolality of approximately 300 mOsm/kg.

CLINICAL PHARMACOLOGY

Olopatadine is a relatively selective histamine H₁ antagonist and an inhibitor of the release of histamine from the mast cells. Decreased chemotaxis and inhibition of eosinophil activation has also been demonstrated. Olopatadine is devoid of effects on alpha-adrenergic, dopaminergic, and muscarinic type 1 and 2 receptors. Systemic bioavailability data upon topical ocular administration of PATADAY™ solution are not available. Following topical ocular administration of olopatadine 0.15% ophthalmic solution in man, olopatadine was shown to have a low systemic exposure. Two studies in normal volunteers (totaling 24 subjects) dosed bilaterally with olopatadine 0.15% ophthalmic solution once every 12 hours for 2 weeks demonstrated plasma concentrations to be generally below the quantitation limit of the assay (< 0.5 ng/mL). Samples in which olopatadine was quantifiable were typically found within 2 hours of dosing and ranged from 0.5 to 1.3 ng/mL. The elimination half-life in plasma following oral dosing was 8 to 12 hours, and elimination was predominantly through renal excretion. Approximately 60–70% of the dose was recovered in the urine as parent drug. Two metabolites, the mono-desmethyl and the N-oxide, were detected at low concentrations in the urine.

CLINICAL STUDIES

Results from clinical studies of up to 12 weeks duration demonstrate that PATADAY™ solution when dosed once a day is effective in the treatment of ocular itching associated with allergic conjunctivitis.

INDICATIONS AND USAGE

PATADAY™ solution is indicated for the treatment of ocular itching associated with allergic conjunctivitis.

CONTRAINDICATIONS

Hypersensitivity to any components of this product.

WARNINGS

For topical ocular use only. Not for injection or oral use.

PRECAUTIONS

Information for Patients

As with any eye drop, to prevent contaminating the dropper tip and solution, care should be taken not to touch the eye lids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use. Patients should be advised not to wear a contact lens if their eye is red. PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% should not be used to treat contact lens related irritation. The preservative in PATADAY™ solution, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses and whose eyes are not red, should be instructed to wait at least ten minutes after instilling PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% before they insert their contact lenses.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Olopatadine administered orally was not carcinogenic in mice and rats in doses up to 500 mg/kg/day and 200 mg/kg/day, respectively. Based on a 40 µL drop size and a 50 kg person, these doses were approximately 150,000 and 50,000 times higher than the maximum recommended ocular human dose (MROHD). No mutagenic potential was observed when olopatadine was tested in an *in vitro* bacterial reverse mutation (Ames) test, an *in vitro* mammalian chromosome aberration assay or an *in vivo* mouse micronucleus test. Olopatadine administered to male and female rats at oral doses of approximately 100,000 times MROHD level resulted in a slight decrease in the fertility index and reduced implantation rate; no effects on reproductive function were observed at doses of approximately 15,000 times the MROHD level.

Pregnancy:

Teratogenic effects: Pregnancy Category C

Olopatadine was found not to be teratogenic in rats and rabbits. However, rats treated at 600 mg/kg/day, or 150,000 times the MROHD and rabbits treated at 400 mg/kg/day, or approximately 100,000 times the MROHD, during organogenesis showed a decrease in live fetuses. In addition, rats treated with 600 mg/kg/day of olopatadine during organogenesis showed a decrease in fetal weight. Further, rats treated with 600 mg/kg/day of olopatadine during late gestation through the lactation period showed a decrease in neonatal survival and body weight.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human responses, this drug should be used in pregnant women only if the potential benefit to the mother justifies the potential risk to the embryo or fetus.

Nursing Mothers:

Olopatadine has been identified in the milk of nursing rats following oral administration. It is not known whether topical ocular administration could result in sufficient systemic absorption to produce detectable quantities in the human breast milk. Nevertheless, caution should be exercised when PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% is administered to a nursing mother.

Pediatric Use:

Safety and effectiveness in pediatric patients below the age of 3 years have not been established.

Geriatric Use:

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

ADVERSE REACTIONS

Symptoms similar to cold syndrome and pharyngitis were reported at an incidence of approximately 10%.

The following adverse experiences have been reported in 5% or less of patients:

Ocular: blurred vision, burning or stinging, conjunctivitis, dry eye, foreign body sensation, hyperemia, hypersensitivity, keratitis, lid edema, pain and ocular pruritus.

Non-ocular: asthenia, back pain, flu syndrome, headache, increased cough, infection, nausea, rhinitis, sinusitis and taste perversion.

Some of these events were similar to the underlying disease being studied.

DOSAGE AND ADMINISTRATION

The recommended dose is one drop in each affected eye once a day.

HOW SUPPLIED

PATADAY™ (olopatadine hydrochloride ophthalmic solution) 0.2% is supplied in a white, oval, low density polyethylene DROP-TAINER® dispenser with a natural low density polyethylene dispensing plug and a white polypropylene cap. Tamper evidence is provided with a shrink band around the closure and neck area of the package.

NDC 0065-0272-25

2.5 mL fill in 4 mL oval bottle

Storage:

Store at 2°C to 25°C (36°F to 77°F)

U.S. Patents Nos. 4,871,865; 4,923,892; 5,116,863; 5,641,805; 6,995,186

Rx Only

ALCON LABORATORIES, INC.
Fort Worth, Texas 76134 USA
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PATANOL®

[pá'tá-nól]

(olopatadine hydrochloride ophthalmic solution) 0.1%

DESCRIPTION

PATANOL® (olopatadine hydrochloride ophthalmic solution) 0.1% is a sterile ophthalmic solution containing olopatadine, a relatively selective H₁-receptor antagonist and inhibitor of histamine release from the mast cell for topical administration to the eyes. Olopatadine hydrochloride is a white, crystalline, water-soluble powder with a molecular weight of 373.88.

Each mL of PATANOL® contains: **Active:** 1.11 mg olopatadine hydrochloride equivalent to 1 mg olopatadine. **Preservative:** benzalkonium chloride 0.01%. **Inactives:** dibasic sodium phosphate; sodium chloride; hydrochloric acid/sodium hydroxide (adjust pH); and purified water. It has a pH of approximately 7 and an osmolality of approximately 300 mOsm/kg.

CLINICAL PHARMACOLOGY

Olopatadine is an inhibitor of the release of histamine from the mast cell and a relatively selective histamine H₁-antagonist that inhibits the *in vivo* and *in vitro* type 1 immediate hypersensitivity reaction including inhibition of histamine induced effects on human conjunctival epithelial cells. Olopatadine is devoid of effects on alpha-adrenergic, dopamine and muscarinic type 1 and 2 receptors. Following topical ocular administration in man, olopatadine was shown to have low systemic exposure. Two studies in normal volunteers (totaling 24 subjects) dosed bilaterally with olopatadine 0.15% ophthalmic solution once every 12 hours for 2 weeks demonstrated plasma concentrations to be generally below the quantitation limit of the assay (<0.5 ng/mL). Samples in which olopatadine was quantifiable were typically found within 2 hours of dosing and ranged from 0.5 to 1.3 ng/mL. The half-life in plasma was approximately 3 hours, and elimination was predominantly through renal excretion. Approximately 60–70% of the dose was recovered in the urine as parent drug. Two metabolites, the mono-desmethyl and the N-oxide, were detected at low concentrations in the urine.

Results from an environmental study demonstrated that PATANOL was effective in the treatment of the signs and symptoms of allergic conjunctivitis when dosed twice daily for up to 6 weeks. Results from conjunctival antigen challenge studies demonstrated that PATANOL®, when subjects were challenged with antigen both initially and up to 8 hours after dosing, was significantly more effective than its vehicle in preventing ocular itching associated with allergic conjunctivitis.

INDICATIONS AND USAGE

PATANOL (olopatadine hydrochloride ophthalmic solution) 0.1% is indicated for the treatment of the signs and symptoms of allergic conjunctivitis.

CONTRAINDICATIONS

PATANOL (olopatadine hydrochloride ophthalmic solution) 0.1% is contraindicated in persons with a known hypersensitivity to olopatadine hydrochloride or any components of PATANOL.

WARNINGS

PATANOL® (olopatadine hydrochloride ophthalmic solution) 0.1% is for topical use only and not for injection or oral use.

PRECAUTIONS

Information for Patients: To prevent contaminating the dropper tip and solution, care should be taken not to touch the eye lids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use.

Patients should be advised not to wear a contact lens if their eye is red. PATANOL® (olopatadine hydrochloride ophthalmic solution) 0.1% should not be used to treat contact lens related irritation. The preservative in PATANOL, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses and whose eyes are not red should be instructed to wait at least ten minutes after instilling PATANOL (olopatadine hydrochloride ophthalmic solution) 0.1% before they insert their contact lenses.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Olopatadine administered orally was not carcinogenic in mice and rats in doses up to 500 mg/kg/day and 200 mg/kg/day, respectively. Based on a 40 µL drop size, these doses were 78,125 and 31,250 times higher than the maximum recommended ocular human dose (MROHD). No mutagenic potential was observed when olopatadine was tested in an *in vitro* bacterial reverse mutation (Ames) test, an *in vitro* mammalian chromosome aberration assay or an *in vivo* mouse micronucleus test. Olopatadine administered to male and female rats at oral doses of 62,500 times MROHD level resulted in a slight decrease in the fertility index and reduced implantation rate; no effects on reproductive function were observed at doses of 7,800 times the maximum recommended ocular human use level.

Pregnancy: Pregnancy Category C

Olopatadine was found not to be teratogenic in rats and rabbits. However, rats treated at 600 mg/kg/day, or 93,750 times the MROHD and rabbits treated at 400 mg/kg/day, or 62,500 times the MROHD, during organogenesis showed a decrease in live fetuses. There are, however, no adequate and well controlled studies in pregnant women. Because animal studies are not always predictive of human responses, this drug should be used in pregnant women only if the potential benefit to the mother justifies the potential risk to the embryo or fetus.

Nursing Mothers: Olopatadine has been identified in the milk of nursing rats following oral administration. It is not known whether topical ocular administration could result in sufficient systemic absorption to produce detectable quantities in the human breast milk. Nevertheless, caution should be exercised when PATANOL® (olopatadine hydrochloride ophthalmic solution) 0.1% is administered to a nursing mother.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 3 years have not been established.

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

ADVERSE REACTIONS

Headaches have been reported at an incidence of 7%. The following adverse experiences have been reported in less than 5% of patients: asthenia, blurred vision, burning or stinging, cold syndrome, dry eye, foreign body sensation, hyperemia, hypersensitivity, keratitis, lid edema, nausea, pharyngitis, pruritus, rhinitis, sinusitis, and taste perversion. Some of these events were similar to the underlying disease being studied.

DOSAGE AND ADMINISTRATION

The recommended dose is one drop in each affected eye two times per day at an interval of 6 to 8 hours.

HOW SUPPLIED

PATANOL (olopatadine hydrochloride ophthalmic solution) 0.1% is supplied as follows: 5 mL in plastic DROP-TAINER® dispenser.

5 mL NDC 0065-0271-05

Storage: Store at 39°F–77°F (4°C–25°C)

Rx Only

U.S. Patents Nos. 5,116,863; 5,641,805.
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SYSTANE®

[sístán]

Lubricant Eye Drops

OTC

DESCRIPTION

SYSTANE® is scientifically formulated to shield eyes from dry eye discomfort so that eyes feel moist and refreshed longer. For the temporary relief of burning and irritation due to dryness of the eye.

Active Ingredients: Polyethylene Glycol 400 0.4% and Propylene Glycol 0.3% as lubricants.

Inactive Ingredients: boric acid, calcium chloride, hydroxypropyl guar, magnesium chloride, polyquaternium-1 as a preservative, potassium chloride, purified water, sodium chloride, zinc chloride. May contain hydrochloric acid and/or sodium hydroxide to adjust pH.

WARNINGS

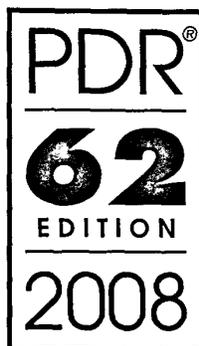
For external use only

Do not use

- if this product changes color or becomes cloudy
- if you are sensitive to any ingredient in this product

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FOREWORD TO THE 62nd EDITION

PDR enters its 62nd year offering a wider array of pharmaceutical reference options than ever before. Long available unabridged—in print, on CD-ROM, and via the Internet—*PDR* also provides essential prescribing information in other forms as well, detailed later in this foreword.

About This Book

Physicians' Desk Reference® is published by Thomson Healthcare in cooperation with participating manufacturers. The *PDR* contains Food and Drug Administration (FDA)-approved labeling for drugs as well as prescription information provided by manufacturers for drugs historically marketed without FDA approval. Some dietary supplements and other products are also included. Each full-length entry provides you with an exact copy of the product's FDA-approved or other manufacturer-supplied labeling. Under the Federal Food, Drug and Cosmetic (FD&C) Act, a drug approved for marketing may be labeled, promoted, and advertised by the manufacturer for only those uses for which the drug's safety and effectiveness have been established. The Code of Federal Regulations Title 21 Section 201.100(d)(1) pertaining to labeling for prescription products requires that for *PDR* content "indications, effects, dosages, routes, methods, and frequency and duration of administration, and any relevant warnings, hazards, contraindications, side effects, and precautions" must be "same in language and emphasis" as the approved labeling for the products. The FDA regards the words *same in language and emphasis* as requiring VERBATIM use of the approved labeling providing such information. Furthermore, information that is emphasized in the approved labeling by the use of type set in a box, or in capitals, boldface, or italics, must be given the same emphasis in *PDR*.

The FDA has also recognized that the FD&C Act does not, however, limit the manner in which a physician may use an approved drug. Once a product has been approved for marketing, a physician may choose to prescribe it for uses or in treatment regimens or patient populations that are not included in approved labeling. The FDA also observes that accepted medical practice includes drug use that is not reflected in approved drug labeling. In the case of over-the-counter dietary supplements, it should be remembered that this information has not been evaluated by the Food and Drug Administration, and that such products are not intended to diagnose, treat, cure, or prevent any disease.

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