DOSAGE AND ADMINISTRATION

α

in patients who develop noticeably increased iris pigmentation, these patients should be
Iris color change may not be noticeable for several months to years. Typically, the brown
are not known.
possibility of increased pigmentation. The long term effects of increased pigmentation
After discontinuation of tafluprost, pigmentation of the iris is likely to be permanent. (5.1)
content in the melanocytes rather than to an increase in the number of melanocytes.
As tafluprost is administered. The pigmentation change is due to increased melanin
5.1 Pigmentation
5 WARNINGS AND PRECAUTIONS
4 CONTRAINDICATIONS

5.2 Eyelash Changes

5.3 Intraocular Inflammation

5.4 Macular Edema

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

6.2 Postmarketing Experience

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.3 Nursing Mothers

8.5 Geriatric Use

8.1 Pregnancy

ZIOPTAN® (tafluprost ophthalmic solution) 0.0015% safely and effectively. See full prescribing information
HIGHLIGHTS OF PRESCRIBING INFORMATION

INDICATIONS AND USAGE

• Ophthalmic solution containing tafluprost

• One drop in the affected eye(s) once daily in the evening. (2)

• ZIOPTAN® (tafluprost ophthalmic solution) 0.0015% is a prostaglandin analog

• Dosage and Administration

• Ophthalmic solution containing tafluprost

CONTRAINDICATIONS

• None. (4)

WARNINGS AND PRECAUTIONS

• Pigmentation

• Pigmentation of the iris, periorbital tissue (eyelid) and eyelashes can occur. Iris

• Eyelash Changes

• Gradual changes to eyelashes including increased length, thickness and number of

• Most common ocular adverse reaction is conjunctival hyperemia (range 4% to

5.2 Eyelash Changes
ZIOPTAN® may gradually change eyelashes and vellus hair in the treated eye. These
changes include increased length, color, thickness, shape and number of lashes. Eyelash
changes are usually reversible upon discontinuation of treatment.

5.3 Intraocular Inflammation
ZIOPTAN® should be used with caution in patients with active intraocular inflammation
(e.g., iritis/uveitis) because the inflammation may be exacerbated.

5.4 Macular Edema
Macular edema, including cystoid macular edema, has been reported during treatment
with prostaglandin F2α analogs. ZIOPTAN® should be used with caution in aphakic
patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with
known risk factors for macular edema.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience
Because clinical studies are conducted under widely varying conditions, adverse 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 practice.
Preservative-containing or preservative-free tafluprost 0.0015% was evaluated in 905
patients in five controlled clinical studies of up to 24-months duration. The most common
adverse reaction observed in patients treated with tafluprost was conjunctival hyperemia
which was reported in a range of 4% to 20% of patients. Approximately 1% of patients
discontinued therapy due to ocular adverse reactions.
Ocular adverse reactions reported at an incidence of ≥2% in these clinical studies
included ocular stinging/irritation (7%), ocular pruritus including allergic conjunctivitis
(5%), cataract (3%), dry eye (3%), ocular pain (3%), eyelash darkening (2%), growth of
eyelashes (2%) and vision blurred (2%).
Nonocular adverse reactions reported at an incidence of 2% to 6% in these clinical studies
in patients treated with tafluprost 0.0015% were headache (6%), common cold (4%),
cough (3%) and urinary tract infection (2%).

6.2 Postmarketing Experience
The following adverse reactions have been identified during postapproval use of tafluprost.
Because postapproval adverse 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.
Respiratory disorders: exacerbation of asthma, dyspnea
Eye disorders: iritis/uveitis
In postmarketing use with prostaglandin analogs, periorbital and lid changes including
deepening of the eyelid sulcus have been observed.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Tafluprost is a colorless to light yellow viscous liquid that is practically insoluble in water. ZIOPTAN® (tafluprost ophthalmic solution) 0.0015% is supplied as a sterile solution of tafluprost with a pH range of 5.5 to 6.7 and an osmolality range of 260 to 300 mOsm/kg.

ZIOPTAN® contains Active: tafluprost 0.015 mg/mL; Inactives: glycerol, sodium dihydrogen phosphate dihydrate, disodium edetate, polysorbate 80, hydrochloric acid and/or sodium hydroxide (to adjust pH) and Water for Injection.

ZIOPTAN® does not contain a preservative.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Tafluprost, a prostaglandin analog is a selective FP prostanoid receptor agonist which is believed to reduce intraocular pressure by increasing uveoscleral outflow. The exact mechanism of action is unknown at this time.

12.3 Pharmacokinetics
Absorption
Following instillation, tafluprost is absorbed through the cornea and is hydrolyzed to the biologically active acid metabolite, tafluprost acid. Following instillation of one drop of the 0.0015% solution once daily into each eye of healthy volunteers, the plasma concentrations of tafluprost acid peaked at a median time of 10 minutes on both Days 1 and 8. The mean plasma Cmax of tafluprost acid were 26 pg/mL and 27 pg/mL on Day 1, and Day 8, respectively. The mean plasma AUC estimates of tafluprost acid were 394 pg·min/mL and 432 pg·min/mL on Day 1 and 8, respectively. The mean plasma AUC estimates of tafluprost acid were 394 pg·min/mL and 432 pg·min/mL on Day 1 and 8, respectively.

Metabolism
Tafluprost, an ester prodrug, is hydrolyzed to its biologically active acid metabolite in the eye. The acid metabolite is further metabolized via fatty acid Oxidation and phase II conjugation.

Elimination
Mean plasma tafluprost acid concentrations were below the limit of quantification of the bioanalytical assay (10 pg/mL) at 30 minutes following topical ocular administration of tafluprost 0.0015% ophthalmic solution.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Tafluprost was not carcinogenic when administered subcutaneously daily for 24 months at doses up to 30 mcg/kg/day in rats and for 18 months at doses up to 100 mcg/kg/day in mice (over 1600 and 1300 times, respectively, the maximum clinical exposure based on plasma AUC).

Tafluprost was not mutagenic or clastogenic in a battery of genetic toxicology studies, including an in vitro microbial mutagenesis assay, an in vitro chromosomal aberration assay in Chinese hamster lung cells, and an in vivo mouse micronucleus assay in bone marrow.

In rats, no adverse effects on mating performance or fertility were observed with intravenous dosing of tafluprost at a dose of 100 mcg/kg/day (over 14000 times the maximum clinical exposure based on plasma Cmax or over 3600 times based on plasma AUC).

14 CLINICAL STUDIES
In clinical studies up to 24 months in duration, patients with open-angle glaucoma or ocular hypertension and baseline pressure of 23 to 26 mm Hg who were treated with ZIOPTAN® dosed once daily in the evening demonstrated reductions in intraocular pressure at 3 and 6 months of 6 to 3 mmHg and 5 to 8 mmHg, respectively.

16 HOW SUPPLIED/STORAGE AND HANDLING
ZIOPTAN® (tafluprost ophthalmic solution) 0.0015% is supplied as a sterile solution in translucent low density polyethylene single-use containers packaged in foil pouches (10 single-use containers per pouch). Each single-use container has 0.3 mL solution corresponding to 0.0045 mg tafluprost.

NDC 17478-609-30; Unit-of-Use Carton of 30. NDC 17478-609-90; Unit-of-Use Carton of 90.

Storage:
Store refrigerated at 2° to 8°C (36° to 46°F).

During shipment ZIOPTAN® may be maintained at temperatures up to 40°C (104°F) for a period not exceeding 2 days. Mail-order prescriptions received after two days of the dispensing date noted in the prescribing label should not be used. Store in the original pouch. After the pouch is opened, the single-use containers may be stored in the opened foil pouch for up to 30 days at room temperature 20° to 25°C (68° to 77°F). Protect from moisture. Write down the date you open the foil pouch in the space provided on the pouch. Discard any unused containers 30 days after first opening the pouch.

17 PATIENT COUNSELING INFORMATION
See FDA-Approved Patient Labeling (Patient Information).

17.1 Nightly Application
Advise patients not to exceed once daily dosing since more frequent administration may decrease the intraocular pressure lowering effect of ZIOPTAN®.

17.2 Handling the Single-Use Container
Advise patients that ZIOPTAN® is a sterile solution that does not contain a preservative. The solution from one individual unit is to be used immediately after opening for administration to one or both eyes. Since sterility cannot be maintained after the individual unit is opened, the remaining contents should be discarded immediately after administration.

17.3 Potential for Pigmentation
Advise patients about the potential for increased brown pigmentation of the iris, which may be permanent. Also inform patients about the possibility of eyelid skin darkening, which may be reversible after discontinuation of ZIOPTAN®.

17.4 Potential for Eyelash Changes
Inform patients of the possibility of eyelash and vellus hair changes in the treated eye during treatment with ZIOPTAN®. These changes may result in a disparity between eyes in length, thickness, pigmentation, number of eyelashes or vellus hairs, and/or direction of eyelash growth. Eyelash changes are usually reversible upon discontinuation of treatment.

17.5 When to Seek Physician Advice
Advise patients that if they develop a new ocular condition (e.g., trauma or infection), experience a sudden decrease in visual acuity, have ocular surgery, or develop any ocular reactions, particularly conjunctivitis and eyelid reactions, they should immediately seek their physician’s advice concerning the continued use of ZIOPTAN®.

17.6 Use with Other Ophthalmic Drugs
If more than one topical ophthalmic drug is being used, the drugs should be administered at least 5 (minutes) between applications.

17.7 Storage Information
Instruct patients on proper storage of cartons, unopened foil pouches, and opened foil pouches [see How Supplied/Storage and Handling (16)]. Recommended storage for cartons and unopened foil pouches is to store refrigerated at 2° to 8°C (36° to 46°F). After the pouch is opened, the single-use containers may be stored in the opened foil pouch for up to 30 days at room temperature 20° to 25°C (68° to 77°F). Protect from moisture.