HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use PROLENSA safely and effectively. See full prescribing information for PROLENSA ophthalmic solution.

PROLENSA® (bromfenac ophthalmic solution), for topical ophthalmic use
Initial U.S. Approval: 1997

---------- INDICATIONS AND USAGE ----------
PROLENSA is a nonsteroidal anti-inflammatory drug (NSAID) indicated for the treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery. (1)

---------- DOSAGE AND ADMINISTRATION ----------
Instill one drop into the affected eye once daily beginning 1 day prior to surgery, continued on the day of surgery, and through the first 14 days postsurgery. (2.1)

---------- DOSAGE FORMS AND STRENGTHS ----------
Topical ophthalmic solution: bromfenac 0.07% (3)

---------- CONTRAINDICATIONS ----------
None (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Sulfite Allergic Reactions (5.1)
- Slow or Delayed Healing (5.2)
- Potential for Cross-Sensitivity (5.3)
- Increased Bleeding Time (5.4)
- Keratitis and Corneal Reactions (5.5)
- Contact Lens Wear (5.6)

---------- ADVERSE REACTIONS ----------
The most commonly reported adverse reactions in 3% to 8% of patients were anterior chamber inflammation, foreign body sensation, eye pain, photophobia, and blurred vision. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Bausch & Lomb Incorporated at 1-800-553-5340 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 01/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

PROLENSA® (bromfenac ophthalmic solution) 0.07% is indicated for the treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosing

One drop of PROLENSA ophthalmic solution should be applied to the affected eye once daily beginning 1 day prior to cataract surgery, continued on the day of surgery, and through the first 14 days of the postoperative period.

2.2 Use with Other Topical Ophthalmic Medications

PROLENSA ophthalmic solution may be administered in conjunction with other topical ophthalmic medications such as alpha-agonists, beta-blockers, carbonic anhydrase inhibitors, cycloplegics, and mydriatics. Drops should be administered at least 5 minutes apart.

3 DOSAGE FORMS AND STRENGTHS

Topical ophthalmic solution: bromfenac 0.07%

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Sulfite Allergic Reactions

PROLENSA ophthalmic solution contains sodium sulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.

5.2 Slow or Delayed Healing

All topical nonsteroidal anti-inflammatory drugs (NSAIDs), including bromfenac, may slow or delay healing. Topical corticosteroids are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.

5.3 Potential for Cross-Sensitivity

There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs, including bromfenac. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

5.4 Increased Bleeding Time

With some NSAIDs, including bromfenac, there exists the potential for increased bleeding time due to interference with platelet aggregation. There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery.

It is recommended that PROLENSA ophthalmic solution be used with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.

5.5 Keratitis and Corneal Reactions

Use of topical NSAIDs may result in keratitis. In some susceptible patients, continued use of topical NSAIDs may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or corneal perforation. These events may be sight threatening. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of topical NSAIDs, including bromfenac, and should be closely monitored for corneal health.

Postmarketing experience with topical NSAIDs suggests that patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases (e.g., dry eye syndrome), rheumatoid arthritis, or repeat ocular surgeries within a short period of time may be at increased risk for corneal adverse events which may become sight threatening. Topical NSAIDs should be used with caution in these patients.

Postmarketing experience with topical NSAIDs also suggests that use more than 24 hours prior to surgery or use beyond 14 days postsurgery may increase patient risk for the occurrence and severity of corneal adverse events.

5.6 Contact Lens Wear

PROLENSA should not be instilled while wearing contact lenses. Remove contact lenses prior to instillation of PROLENSA. The preservative in PROLENSA, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of PROLENSA.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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

The most commonly reported adverse reactions following use of PROLENSA following cataract surgery include: anterior chamber inflammation, foreign body sensation, eye pain, photophobia, and blurred vision. These reactions were reported in 3% to 8% of patients.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Treatment of rats at oral doses up to 0.9 mg/kg/day (systemic exposure 90 times the systemic exposure predicted from the recommended human ophthalmic dose [RHOD] assuming the human systemic concentration is at the limit of quantification) and rabbits at oral doses up to 7.5 mg/kg/day (150 times the predicted human systemic exposure) produced no treatment-related malformations in reproduction studies. However, embryofetal lethality and maternal toxicity were produced in rats and rabbits at 0.9 mg/kg/day and 7.5 mg/kg/day, respectively. In rats, bromfenac treatment caused delayed parturition at 0.3 mg/kg/day (30 times the predicted human exposure), and caused dystocia, increased neonatal mortality, and reduced postnatal growth at 0.9 mg/kg/day.

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Because of the known effects of prostaglandin biosynthesis-inhibiting drugs on the fetal cardiovascular system (closure of ductus arteriosus), the use of PROLENSA ophthalmic solution during late pregnancy should be avoided.

8.3 Nursing Mothers

Caution should be exercised when PROLENSA ophthalmic solution is administered to a nursing woman.

8.4 Pediatric Use

Safety and efficacy in pediatric patients below the age of 18 years have not been established.

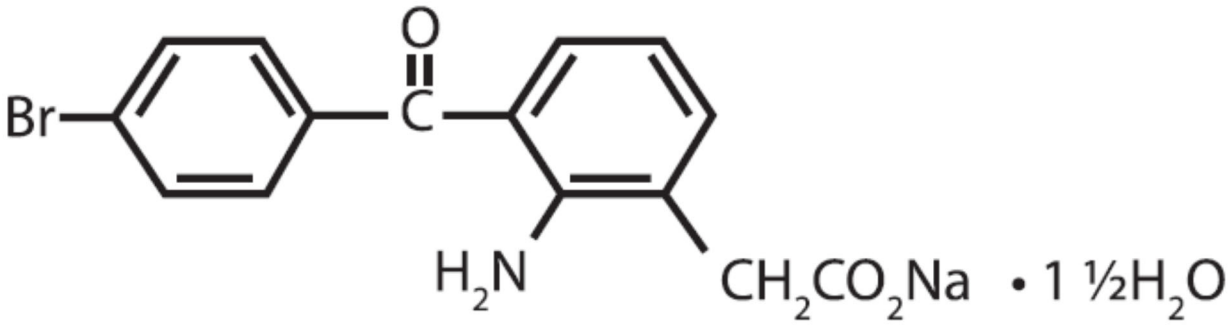
8.5 Geriatric Use

There is no evidence that the efficacy or safety profiles for PROLENSA differ in patients 70 years of age and older compared to younger adult patients.

11 DESCRIPTION

PROLENSA® (bromfenac ophthalmic solution) 0.07% is a sterile, topical, nonsteroidal anti-inflammatory drug (NSAID) for ophthalmic use. Each mL of PROLENSA contains 0.805 mg bromfenac sodium sesquihydrate (equivalent to 0.7 mg bromfenac free acid). The USAN name for bromfenac sodium sesquihydrate is bromfenac sodium. Bromfenac sodium is

designated chemically as sodium [2-amino-3-(4-bromobenzoyl) phenyl] acetate sesquihydrate, with an empirical formula of $C_{15}H_{11}BrNNaO_3 \bullet 1½H_2O$. The chemical structure for bromfenac sodium sesquihydrate is:



Bromfenac sodium is a yellow to orange crystalline powder. The molecular weight of bromfenac sodium is 383.17. PROLENSA ophthalmic solution is supplied as a sterile aqueous 0.07% solution, with a pH of 7.8. The osmolality of PROLENSA ophthalmic solution is approximately 300 mOsmol/kg.

Each mL of PROLENSA ophthalmic solution contains:
Active: Each mL contains bromfenac sodium sesquihydrate 0.0805%, which is equivalent to bromfenac free acid 0.07%.
Inactives: boric acid, edetate disodium, povidone, sodium borate, sodium sulfite, tyloxapol, sodium hydroxide to adjust pH, and water for injection, USP.
Preservative: benzalkonium chloride 0.005%

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Bromfenac is a nonsteroidal anti-inflammatory drug (NSAID) that has anti-inflammatory activity. The mechanism of its action is thought to be due to its ability to block prostaglandin synthesis by inhibiting cyclooxygenase (COX) 1 and 2. Prostaglandins have been shown in many animal models to be mediators of certain kinds of intraocular inflammation. In studies performed in animal eyes, prostaglandins have been shown to produce disruption of the blood-aqueous humor barrier, vasodilation, increased vascular permeability, leukocytosis, and increased intraocular pressure.

12.3 Pharmacokinetics

The plasma concentration of bromfenac following ocular administration of PROLENSA (bromfenac ophthalmic solution) 0.07% in humans is unknown. Based on the maximum proposed dose of one drop to each eye (0.035 mg) and PK information from other routes of administration, the systemic concentration of bromfenac is estimated to be below the limit of quantification (50 ng/mL) at steady-state in humans.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term carcinogenicity studies in rats and mice given oral doses of bromfenac up to 0.6 mg/kg/day (systemic exposure 30 times the systemic exposure predicted from the recommended human ophthalmic dose [RHOD] assuming the human systemic concentration is at the limit of quantification) and 5 mg/kg/day (340 times the predicted human systemic exposure), respectively, revealed no significant increases in tumor incidence.

Bromfenac did not show mutagenic potential in various mutagenicity studies, including the reverse mutation, chromosomal aberration, and micronucleus tests.

Bromfenac did not impair fertility when administered orally to male and female rats at doses up to 0.9 mg/kg/day and 0.3 mg/kg/day, respectively (systemic exposure 90 and 30 times the predicted human exposure, respectively).

14 CLINICAL STUDIES

14.1 Ocular Inflammation and Pain

Bromfenac 0.07% QD for the treatment of postoperative inflammation and reduction of ocular pain was evaluated in two multi-center, randomized, double-masked, parallel-group, and placebo (vehicle)-controlled studies. Patients undergoing cataract surgery self-administered bromfenac 0.07% or vehicle once daily, beginning 1 day prior to surgery, continuing on the morning of surgery and for 14 days after surgery. Complete clearance of ocular inflammation (0 cell and no flare) was assessed on Days 1, 3, 8, and 15 postsurgery using slit lamp biomicroscopy. The pain score was self-reported. The primary efficacy endpoint was the proportion of subjects who had complete clearance of ocular inflammation by Day 15. In the intent-to-treat analyses from both assessments, complete clearance at Day 8 and Day 15, bromfenac 0.07% was superior to vehicle as shown in the following table.

Proportion of Subjects with Cleared Ocular Inflammation (0 cells and no flare)				
Study	Visit	Bromfenac 0.07%	Vehicle	Difference (%) (Asymptotic 95% CI)
Study 1	At Day 8	27/112 (24.1%)	7/108 (6.5%)	17.6 (8.4, 26.8)
	At Day 15	51/112 (45.5%)	14/108 (13.0%)	32.5 (21.4, 43.8)
Study 2	At Day 8	33/110 (30.0%)	14/110 (12.7%)	17.3 (6.7, 27.9)
	At Day 15	50/110 (45.5%)	30/110 (27.3%)	18.2 (5.7, 30.7)
Proportion of Subjects Who Were Pain Free				
Study	Visit	Bromfenac 0.07%	Vehicle	Difference (%) (Asymptotic 95% CI)
Study 1	At Day 1	91/112 (81.3%)	47/108 (43.5%)	37.7 (25.9, 49.6)
Study 2	At Day 1	84/110 (76.4%)	61/110 (55.5%)	20.9 (8.7, 33.1)

16 HOW SUPPLIED/STORAGE AND HANDLING

PROLENSA® (bromfenac ophthalmic solution) 0.07% is supplied in a white LDPE plastic squeeze bottle with a 15 mm LDPE white dropper tip and 15 mm polypropylene gray cap as follows:

- 3 mL in a 7.5 mL container (NDC 24208-602-03)

Storage: Store at 15ºC to 25ºC (59ºF to 77ºF).

17 PATIENT COUNSELING INFORMATION

Slowed or Delayed Healing

Advise patients of the possibility that slow or delayed healing may occur while using NSAIDs.

Sterility of Dropper Tip

Advise patients to replace bottle cap after using and to not touch dropper tip to any surface, as this may contaminate the contents.

Advise patients that a single bottle of PROLENSA be used to treat only one eye.

Concomitant Use of Contact Lenses

Advise patients to remove contact lenses prior to instillation of PROLENSA. The preservative in PROLENSA, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of PROLENSA.

Concomitant Topical Ocular Therapy

If more than one topical ophthalmic medication is being used, the medicines should be administered at least 5 minutes apart.

Distributed by:
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Bridgewater, NJ 08807 USA

Under License From:
Senju Pharmaceutical Co., Ltd.
Osaka, Japan 541-0046

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