This carton has not yet been confirmed for commercialization.
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### Full Prescribing Information

**1. Indications and Usage**

Bromfenac Ophthalmic Solution: 0.09% 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

For the treatment of postoperative inflammation in patients who have undergone cataract extraction, one drop of bromfenac ophthalmic solution should be applied to the affected eye once daily beginning 1 day prior to surgery, continued on the day of surgery and through the first 14 days post-surgery (2.1).

**2.2.** Use with Other Topical Ophthalmic Medications

Bromfenac 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. Adverse Reactions**

Topical ophthalmic solution: bromfenac 0.09%.

**4. Contraindications**

None.

**5. Warnings and Precautions**

**5.1.** Sulfite Allergic Reactions

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 asthmatics than in non-asthmatic people.

**5.2.** Slow or Delayed Healing

Topical non-steroidal anti-inflammatory drugs (NSAIDs) may slow or delay healing.

**5.3.** Potential for Cross-Sensitivity

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

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**NOTE:** Pharmacode is vendor-specific information and may vary.
6 ADVERSE REACTIONS

6.1 Clinical Trial Experience

The most commonly reported adverse experiences reported following use of bromfenac after cataract surgery include: abnormal sensation in eye, conjunctival hyperemia, eye irritation (including burning/stinging), eye pain, eye pruritus, eye redness, headache, and iritis. These events were reported in 2-7% of patients.

6.2 Postmarketing Experience

The following events have been identified during post-marketing use of bromfenac ophthalmic solution 0.09% in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The events, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to topical bromfenac ophthalmic solution 0.09% or a combination of these factors, include corneal erosion, corneal perforation, corneal thinning, and epithelial breakdown. [see Warnings and Precautions (6)]

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects: Pregnancy Category C.

Reproduction studies performed in rats at oral doses up to 0.9 mg/kg/day (1300 times the recommended human ophthalmic dose [RHOD]) and in rabbits at oral doses up to 7.6 mg/kg/day (11,000 times RHOD) revealed no evidence of teratogenicity due to bromfenac. However, 0.9 mg/kg/day in rats caused embryo-fetal lethality, increased neonatal mortality, and reduced postnatal growth. Pregnant rabbits treated with 7.5 mg/kg/day caused increased post-implantation loss.

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.

Nonteratogenic Effects:

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

8.3 Nursing Mothers

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

8.4 Pediatric Use

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

8.5 Geriatric Use

There is no evidence that the efficacy or safety profiles for bromfenac ophthalmic solution differ in patients 65 years of age and older compared to younger adult patients.

11 DESCRIPTION

Bromfenac ophthalmic solution 0.09% is a sterile, topical, non-steroidal anti-inflammatory drug (NSAID) for ophthalmic use. Each ml of bromfenac ophthalmic solution 0.09% contains 1.035 mg bromfenac sodium sesquihydrate (equivalent to 0.9 mg bromfenac free acid). Bromfenac sodium sesquihydrate is designated chemically as sodium 2-amino-3-(4-bromobenzenzoxy) phenyl acetate sesquihydrate, with an empirical formula of C_{29}H_{34}BrNaNO_{12} \cdot 3/2 H_{2}O. The structural formula for bromfenac sodium sesquihydrate is:

```
  Br
  CH_{2}CO_{2}Na \cdot 3/2 H_{2}O

\atom{Br}
\text{Br} \text{N}
\text{CH}_{3}
\text{CO}_{2}\text{Na} \cdot 3/2 \text{H}_{2}\text{O}
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Bromfenac sodium sesquihydrate is a yellow to orange crystalline powder. The molecular weight of bromfenac sodium sesquihydrate is 583.17. Bromfenac Ophthalmic Solution is supplied as a sterile aqueous 0.09% solution, with a pH between 8.0 and 8.6. The osmolality of Bromfenac Ophthalmic Solution is between 270 and 350 mOsm/kg.

Each ml of Bromfenac Ophthalmic Solution contains:

- Active: bromfenac sodium sesquihydrate 0.1035%
- Preservative: benzalkonium chloride (0.05 mg/ml)
- Inactives: boric acid, edetate disodium dihydrogen, polysorbate 80, povidone, sodium borate, sodium sulfite antioxidant, sodium hydroxide to adjust pH and water for injection.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Bromfenac is a non-steroidal 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 1 and 2.

Prostaglandins have been shown in many animal models to be mediators of certain kinds of intracocular 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 0.09% bromfenac ophthalmic solution in humans is unknown. Based on the maximum proposed dose of one drop to the eye (0.045 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 0.8 mg/kg/day (900 times the recommended human ophthalmic dose [RHOD] of 1.67 mg/kg in 60 kg person on a mg/kg basis, assuming 100% absorbed) and 5 mg/kg/day (750 times RHOD), 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 (1300 and 450 times RHOD, respectively).

14 CLINICAL STUDIES

14.1 Ocular inflammation and pain following cataract surgery

Clinical efficacy was evaluated in three randomized, double-masked, placebo controlled trials in which subjects requiring cataract surgery were assigned to bromfenac ophthalmic solution or placebo. Patients were dosed with one drop per eye starting the day before surgery and continuing for 14 days. The primary endpoint was clearing of ocular inflammation by day 15. An additional efficacy endpoint was the number of patients who were pain free on day 1 after cataract surgery.

In 2 of the 3 studies, bromfenac ophthalmic solution had statistically significant higher incidence of completely clearing inflammation (46-47% vs. 25-29%) and also had a statistically significant higher incidence of subjects that were pain free at day 1 post cataract surgery (82-89% vs. 51-71%).

16 HOW SUPPLIED/STORAGE AND HANDLING

Bromfenac Ophthalmic Solution 0.09% is supplied in a white opaque LDPE ophthalmic bottle with white translucent LDPE ophthalmic dropper and grey opaque HDPE ophthalmic cap with seal tape as follows:

- 1.7 ml in 5 ml bottle as a Single pack (1 bottle / carton) - NDC 60806-0595-5
- 1.7 ml in 5 ml bottle as a Twin pack (2 bottles / carton) - NDC 60806-0595-6

STORAGE

Store at 20° - 25°C (68° - 77°F) [See USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

17.1 Solved or Delayed Healing

Patients should be advised of the possibility that slow or delayed healing may occur while using NSAIDs.

17.2 Sterility of Dropper Tip

Patients should be advised not to touch dropper tip to any surface, as this may contaminate the contents.

17.3 Concomitant Use of Contact Lenses

Contact lenses should not be worn during the use of this product.

17.4 Concomitant Topical Ocular Therapy

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

Manufactured by: Manufactured for:
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/s/

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09/19/2013

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09/23/2013