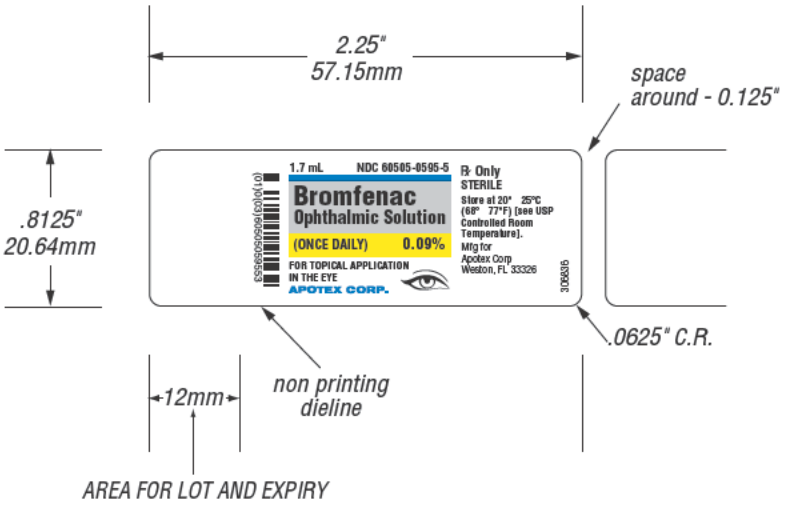


Enlarged 200%

1.7 mL NDC 60505-0595-5

Bromfenac
Ophthalmic Solution

(ONCE DAILY) 0.09%

FOR TOPICAL APPLICATION
IN THE EYE
APOTEX CORP.

(01)0(03)60505059553

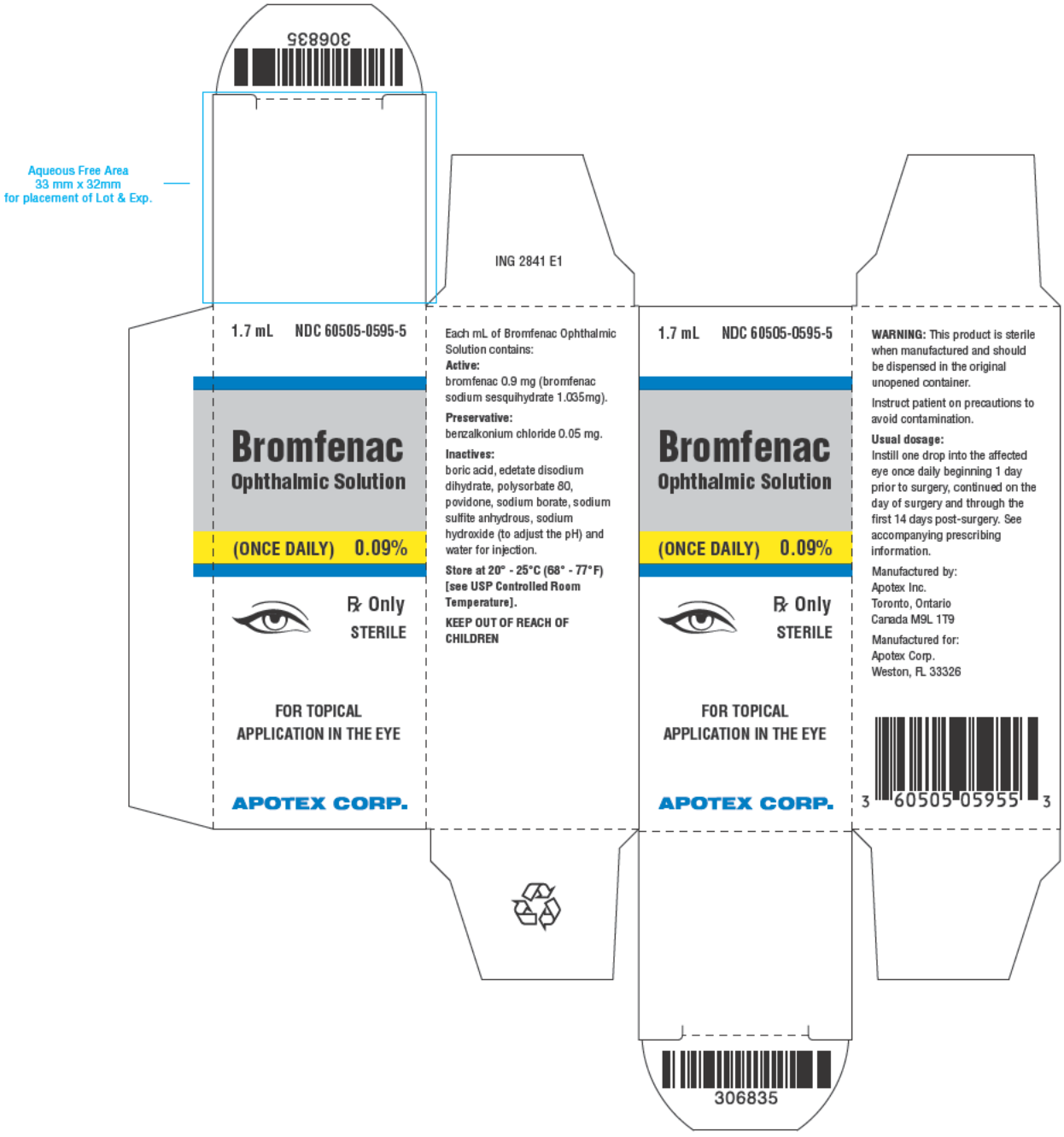
℞ **Only**
STERILE
Store at 20° - 25°C (68° - 77°F) [see USP Controlled Room Temperature].
Mfg for:
Apotex Corp.
Weston, FL 33326

306836

(b) (4)

This carton has not yet been confirmed for commercialization.

Reference ID: 3376099


306835
Aqueous Free Area
33 mm x 32mm
for placement of Lot & Exp.
ING 2841 E1
1.7 mL NDC 60505-0595-5
Bromfenac
Ophthalmic Solution
(ONCE DAILY) 0.09%
℞ Only
STERILE
FOR TOPICAL
APPLICATION IN THE EYE
APOTEX CORP.
Each mL of Bromfenac Ophthalmic Solution contains:
Active:
bromfenac 0.9 mg (bromfenac sodium sesquihydrate 1.035mg).
Preservative:
benzalkonium chloride 0.05 mg.
Inactives:
boric acid, edetate disodium dihydrate, polysorbate 80, povidone, sodium borate, sodium sulfite anhydrous, sodium hydroxide (to adjust the pH) and water for injection.
Store at 20° - 25°C (68° - 77°F) [see USP Controlled Room Temperature].
KEEP OUT OF REACH OF CHILDREN
1.7 mL NDC 60505-0595-5
Bromfenac
Ophthalmic Solution
(ONCE DAILY) 0.09%
℞ Only
STERILE
FOR TOPICAL
APPLICATION IN THE EYE
APOTEX CORP.
WARNING: This product is sterile when manufactured and should be dispensed in the original unopened container.
Instruct patient on precautions to avoid contamination.
Usual dosage:
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 post-surgery. See accompanying prescribing information.
Manufactured by:
Apotex Inc.
Toronto, Ontario
Canada M9L 1T9
Manufactured for:
Apotex Corp.
Weston, FL 33326
3 60505 05955 3
306835

NOTE: Pharmacode is vendor specific information and may vary.

266 mm

133 mm

26 mm

200 mm

321809

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Bromfenac Ophthalmic Solution, 0.09% safely and effectively. See full prescribing information for Bromfenac Ophthalmic Solution, 0.09%.

Bromfenac Ophthalmic Solution, 0.09%
Initial U.S. Approval: 1997

----------INDICATIONS AND USAGE----------

Bromfenac Ophthalmic Solution 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 extraction (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 post-surgery (2.1).

--------DOSAGE FORMS AND STRENGTHS--------

Topical ophthalmic solution: bromfenac 0.09% (3)

----------WARNINGS AND PRECAUTIONS----------

- Sulfite Allergic Reactions (5.1)
- Slow or Delayed Healing (5.2)
- Potential for cross-sensitivity (5.3)
- Increase bleeding of ocular tissues (5.4)
- Corneal effects including keratitis (5.5)
- Contact Lens Wear (5.6)

----------ADVERSE REACTIONS----------

The most commonly reported adverse reactions in 2-7% of patients were abnormal sensation in eye, conjunctival hyperemia and eye irritation (including burning/stinging) (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Apotex Corp. at 1-800-667-4708 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

See 17 for PATIENT COUNSELING INFORMATION

Revised: 07/2013

FULL PRESCRIBING INFORMATION: CONTENTS*

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

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 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

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 DOSAGE FORMS AND STRENGTHS

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 asthmatic than in non asthmatic people.

5.2 Slow or Delayed Healing

All topical non steroidal anti-inflammatory drugs (NSAIDs) 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, phenyl acetic acid derivatives, and other NSAIDs. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

5.4 Increased Bleeding Time

With some NSAIDs, 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 bromfenac 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 and should be closely monitored for corneal health.

Post-marketing 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.

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

5.6 Contact Lens Wear

Bromfenac ophthalmic solution should not be administered while wearing contact lenses.

NOTE: Pharmacode is vendor specific information and may vary.

266 mm

133 mm

26 mm

200 mm

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 (5)]

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 7.5 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

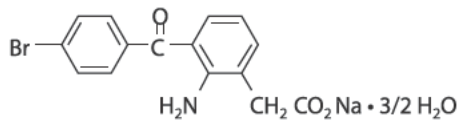
Safety and efficacy in pediatric patients below the age of 18 have not been established.

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-bromobenzoyl) phenyl acetate sesquihydrate, with an empirical formula of $C_{15}H_{11}BrNNaO_3 \cdot {}^3/_2\ H_2O$. The structural structure for bromfenac sodium sesquihydrate is:



Bromfenac sodium sesquihydrate is a yellow to orange crystalline powder. The molecular weight of bromfenac sodium sesquihydrate is 383.17. Bromfenac Ophthalmic Solution is supplied as a sterile aqueous 0.09% solution, with a pH between 8.0 to 8.6. The osmolality of Bromfenac Ophthalmic Solution is between 270 to 330 mOsmol/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 dihydrate, polysorbate 80, povidone, sodium borate, sodium sulfite anhydrous, sodium hydroxide to adjust pH and water for injection.

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 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 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 0.6 mg/kg/day (900 times the recommended human ophthalmic dose [RHOD] of 1.67 mcg/kg in 60 kg person on a mg/kg/basis, assuming 100% absorbed) and 5 mg/kg/day (7500 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 (83-89% 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 sealing tape as follows:

1.7 mL in 5 mL bottle as a Single pack (1 bottle / carton) - NDC 60505-0595-5

1.7 mL in 5 mL bottle as a Twin pack (2 bottles / carton) - NDC 60505-0595-6

STORAGE

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

17 PATIENT COUNSELING INFORMATION

17.1 Slowed 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 to not 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:
Apotex Inc.	Apotex Corp.
Toronto, Ontario	Weston, FL
Canada M9L 1T9	33326

321809 Revised: 07/2013

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

BEVERLY WEITZMAN
09/19/2013

JOHN F GRACE
09/23/2013