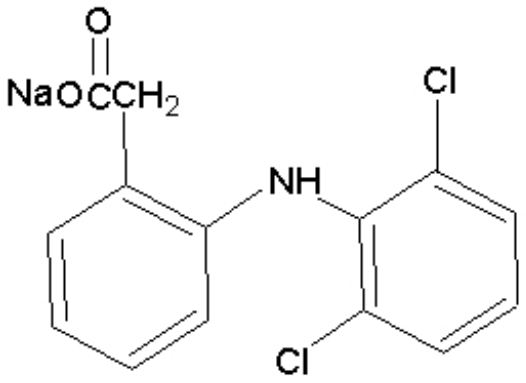
DICLOFENAC SODIUM- diclofenac sodium solution/ drops
Bausch & Lomb Incorporated

Diclofenac Sodium Ophthalmic
Solution, 0.1% (Sterile)

DESCRIPTION

Diclofenac Sodium Ophthalmic Solution 0.1% is a sterile, topical, non-steroidal, anti-inflammatory product for ophthalmic use. Diclofenac Sodium is designated chemically as 2-[(2,6-dichlorophenyl)amino] benzeneacetic acid, monosodium salt, with an empirical formula of $C_{14}H_{10}CI_2NO_2$ Na. The structural formula of diclofenac sodium is:



Diclofenac Sodium Ophthalmic is available as a sterile solution, which contains diclofenac sodium 0.1% (1 mg/mL).

Inactive Ingredients: Boric acid, edetate disodium (1 mg/mL), polyoxyl 35 castor oil, purified water, sorbic acid (2 mg/mL), and tromethamine.

Diclofenac Sodium is a faintly yellow-white to light-beige, slightly hygroscopic crystalline powder. It is freely soluble in methanol, sparingly soluble in water, very slightly soluble in acetonitrile, and insoluble in chloroform and in 0.1N hydrochloric acid. Its molecular weight is 318.14. Diclofenac Sodium Ophthalmic 0.1% is an iso-osmotic solution with an osmolality of about 300 mOsmol/1000 g, buffered at approximately pH 7.2. Diclofenac Sodium Ophthalmic solution has a faint characteristic odor of castor oil.

CLINICAL PHARMACOLOGY

Pharmacodynamics

Diclofenac Sodium is one of a series of phenylacetic acids that has demonstrated anti-inflammatory and analgesic properties in pharmacological studies. It is thought to inhibit the enzyme cyclooxygenase, which is essential in the biosynthesis of prostaglandins.

Animal Studies

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.

Pharmacokinetics

Results from a bioavailability study established that plasma levels of diclofenac following ocular instillation of two drops of Diclofenac Sodium Ophthalmic to each eye were below the limit of quantification (10 ng/mL) over a 4-hour period.

This study suggests that limited, if any, systemic absorption occurs with Diclofenac Sodium Ophthalmic.

Clinical Trials

Postoperative Anti-Inflammatory Effects:

In two double-masked, controlled, efficacy studies of postoperative inflammation, a total of 206 cataract patients were treated with Diclofenac Sodium Ophthalmic and 103 patients were treated with vehicle placebo. Diclofenac Sodium Ophthalmic was favored over vehicle placebo over a 2-week period for the clinical assessments of inflammation as measured by anterior chamber cells and flare.

In double-masked, controlled studies of corneal refractive surgery (radial keratotomy (RK) and laser photorefractive keratectomy (PRK)) patients were treated with Diclofenac Sodium Ophthalmic and/or vehicle placebo. The efficacy of Diclofenac Sodium Ophthalmic given before and shortly after surgery was favored over vehicle placebo during the 6-hour period following surgery for the clinical assessments of pain and photophobia. Patients were permitted to use a hydrogel soft contact lens with Diclofenac Sodium Ophthalmic for up to three days after PRK.

INDICATIONS AND USAGE

Diclofenac Sodium Ophthalmic is indicated for the treatment of postoperative inflammation in patients who have undergone cataract extraction and for the temporary relief of pain and photophobia in patients undergoing corneal refractive surgery.

CONTRAINDICATIONS

Diclofenac Sodium Ophthalmic is contraindicated in patients who are hypersensitive to any component of the medication.

WARNINGS

The refractive stability of patients undergoing corneal refractive procedures and treated with Diclofenac Sodium Ophthalmic has not been established. Patients should be monitored for a year following use in this setting.

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

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

PRECAUTIONS:

General

All topical nonsteroidal 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.

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 infiltrates, corneal erosion, corneal ulceration, and 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.

Postmarketing experience with topical NSAIDs suggests that patients experiencing complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface disease (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 post surgery may increase patient risk for occurrence and severity of corneal adverse events.

It is recommended that Diclofenac Sodium Ophthalmic, like other NSAIDs, be used with caution in patients with known bleeding tendencies or who are receiving other medications, which may prolong bleeding time. Use of the same bottle for both eyes is not recommended with topical eye drops that are used in association with surgery.

Results from clinical studies indicate that Diclofenac Sodium Ophthalmic has no significant effect upon ocular pressure. However, elevations in intraocular pressure may occur following cataract surgery.

Information for Patients

Except for the use of a bandage hydrogel soft contact lens during the first 3 days following refractive surgery, Diclofenac Sodium Ophthalmic should not be used by patients currently wearing soft contact lenses due to adverse events that have occurred in other circumstances.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term carcinogenicity studies in rats given Diclofenac Sodium Ophthalmic in oral doses up to 2 mg/kg/day (approximately 500 times the human topical ophthalmic dose) revealed no significant increases in tumor incidence. A 2-year carcinogenicity study conducted in mice employing oral Diclofenac Sodium Ophthalmic up to 2 mg/kg/day did not reveal any oncogenic potential. Diclofenac Sodium Ophthalmic did not show mutagenic potential in various mutagenicity studies including the Ames test. Diclofenac Sodium Ophthalmic administered to male and female rats at 4 mg/kg/day (approximately 1000 times the human topical ophthalmic dose) did not affect fertility.

Geriatric Use

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

PREGNANCY

Teratogenic Effects

Pregnancy Category C. Reproduction studies performed in mice at oral doses up to 5,000 times (20 mg/kg/day) and in rats and rabbits at oral doses up to 2,500 times (10 mg/kg/day) the human topical dose have revealed no evidence of teratogenicity due to Diclofenac Sodium Ophthalmic despite the induction of maternal toxicity and fetal toxicity. In rats, maternally toxic doses were associated with dystocia, prolonged gestation, reduced fetal weights and growth, and reduced fetal survival. Diclofenac Sodium Ophthalmic has been shown to cross the placental barrier in mice and rats.

There are, however, 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 clearly needed.

Non-teratogenic Effects

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

Nursing Women

It is not known whether topical ophthalmic administration of Diclofenac Sodium Ophthalmic could result in sufficient systemic absorption to produce detectable quantities in breast milk. Because many drugs are excreted in human milk, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

Ocular: Transient burning and stinging were reported in approximately 15% of patients across studies with the use of Diclofenac Sodium Ophthalmic. In cataract surgery studies, keratitis was reported in up to 28% of patients receiving Diclofenac Sodium Ophthalmic, although in many of these cases keratitis was initially noted prior to the initiation of treatment. Elevated intraocular pressure following cataract surgery was reported in approximately 15% of patients undergoing cataract surgery.

Lacrimation complaints were reported in approximately 30% of case studies undergoing incisional refractive surgery. The following adverse reactions were reported in approximately 10% or less of the patients: abnormal vision, acute elevated IOP, blurred vision, conjunctivitis, corneal deposits, corneal edema, corneal opacity, corneal lesions, discharge, eyelid swelling, eye pain, injection (redness), iritis, irritation, itching, lacrimation disorder and ocular allergy.

Systemic: The following adverse reactions were reported in 3% or less of the patients: abdominal pain, asthenia, chills, dizziness, facial edema, fever, headache, insomnia, nausea, pain, rhinitis, viral infection, and vomiting.

Clinical Practice: The following reactions have been identified during postmarketing use of topical Diclofenac Sodium Ophthalmic Solution, 0.1% in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to topical Diclofenac Sodium Ophthalmic Solution, 0.1%, or a combination of these factors, include corneal erosion, corneal infiltrates, corneal perforation, corneal thinning, corneal ulceration, and epithelial breakdown **(see PRECAUTIONS, General).**

OVERDOSAGE

Overdosage will not ordinarily cause acute problems. If Diclofenac Sodium Ophthalmic is accidentally ingested, fluids should be taken to dilute the medication.

DOSAGE AND ADMINISTRATION

Cataract Surgery: One drop of Diclofenac Sodium Ophthalmic should be applied to the affected eye, 4 times daily beginning 24 hours after cataract surgery and continuing throughout the first 2 weeks of the post operative period.

Corneal Refractive Surgery: One or two drops of Diclofenac Sodium Ophthalmic should be applied to the operative eye within the hour prior to corneal refractive surgery. Within 15 minutes after surgery, one or two drops should be applied to the operative eye and continued 4 times daily for up to 3 days.

HOW SUPPLIED

Diclofenac Sodium Ophthalmic 0.1% (1 mg/mL) Sterile Solution is supplied in a low-density polyethylene (LDPE) white bottle with a LDPE Dropper Tip. The 2.5 mL fill and the 5 mL fill are supplied in a 7.5 mL size bottle.

2.5 mL NDC 24208-457-25
5 mL NDC 24208-457-05

Store at 20°C to 25°C (68° to 77°F). Protect from light.

Dispense in original, unopened container only.

Rx only

Revised: November 2012

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Tampa, Florida 33637
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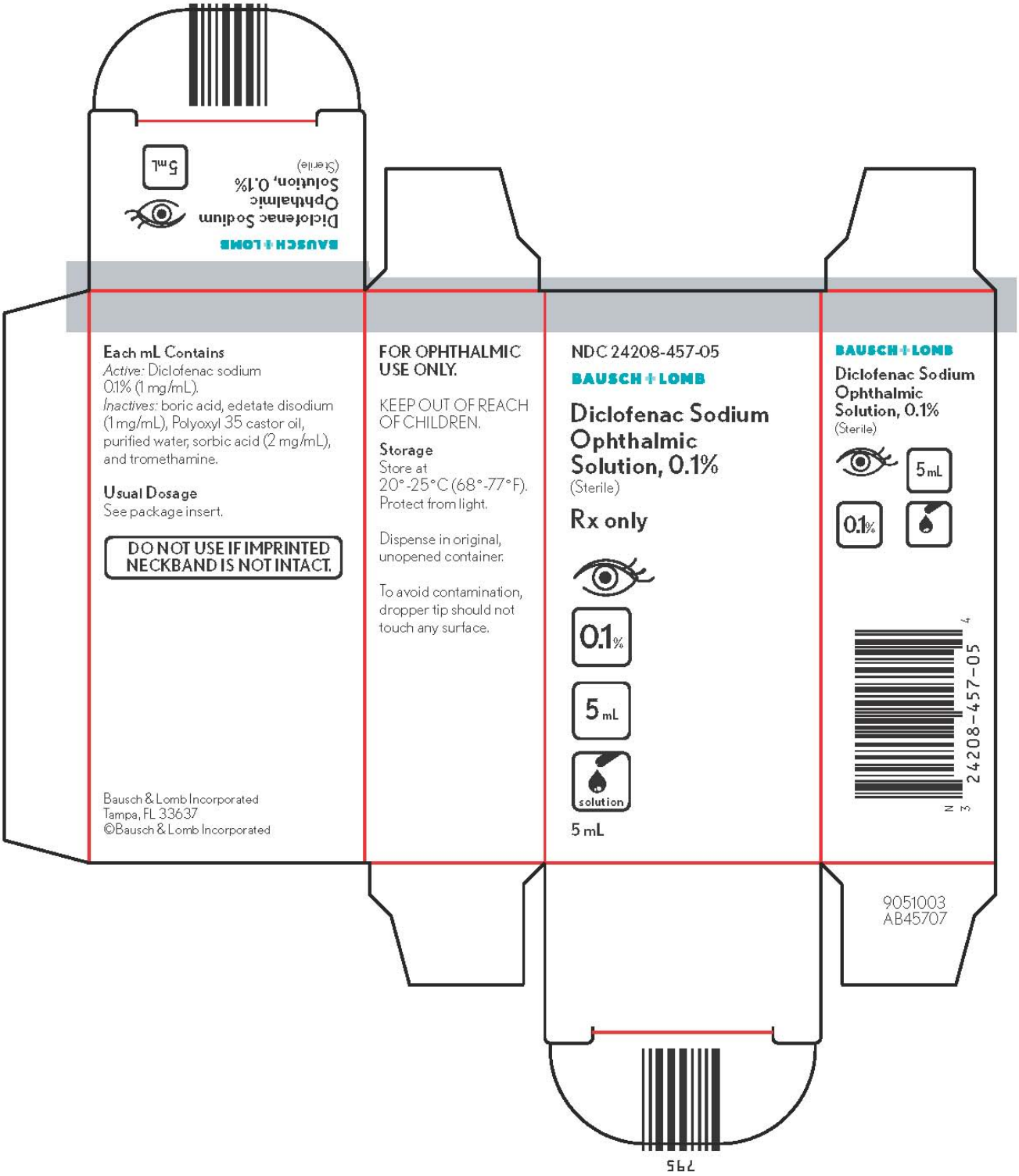
Principal Display Panel



NDC 24208-457-05

Bausch & Lomb

Diclofenac Sodium Ophthalmic Solution, 0.1% (Sterile)

Rx only

[icon- eye] [icon- 0.1%] [icon- solution] [icon- 5 mL]

5 mL

DICLOFENAC SODIUM

diclofenac sodium solution/ drops

Product Information

Product Type	HUMAN PRESCRIPTION DRUG LABEL	**Item Code (Source)**	NDC:24208-457
Route of Administration	OPHTHALMIC	**DEA Schedule**	

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
DICLOFENAC SODIUM (DICLOFENAC)	DICLOFENAC SODIUM	1 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
BORIC ACID	
EDETATE DISODIUM	1 mg in 1 mL
POLYOXYL 35 CASTOR OIL	
WATER	
SORBIC ACID	2 mg in 1 mL
TROMETHAMINE	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:24208-457-05	1 in 1 CARTON		
1		5 mL in 1 BOTTLE, DROPPER		
2	NDC:24208-457-25	1 in 1 CARTON		
2		2.5 mL in 1 BOTTLE, DROPPER		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA078792	12/28/2007	

Labeler - Bausch & Lomb Incorporated (196603781)

Establishment

Name	Address	ID/FEI	Business Operations
Bausch & Lomb Incorporated		807927397	MANUFACTURE(24208-457)

Establishment

Name	Address	ID/FEI	Business Operations
Esteve Quimca S.A.		460940861	API MANUFACTURE(24208-457)