Diclofenac Sodium Ophthalmic Solution, 0.1%

Description
Diclofenac Sodium Ophthalmic Solution, 0.1% is a sterile, topical, nonsteroidal, anti-inflammatory product for ophthalmic use. Diclofenac Sodium is designated chemically as 2-(2,6-dichlorophenyl)benzenacetic acid, monosodium salt, with an empirical formula of C_{13}H_{12}Cl_{2}NO_{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), polysorbate 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 acetone, and insoluble in chloroform and anhydrous ethanol. Its molecular weight is 318.14. Diclofenac Sodium Ophthalmic 0.1% is an isotonic 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 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 intracocular pressure.

Pharmacokinetics
Results from a bioavailability study established that plasma levels of diclofenac following oral administration 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 203 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 hydrogen peroxide 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 retractive stability of patients undergoing corneal refractive procedures and treated with Diclofenac Sodium 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 derangement, 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.
DICLOFENAC SODIUM Ophthalmic 0.1% (1 mg/mL) Sterile Solution

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Dispense in original, unopened container only.

Store at 20°-25°C (68°-77°F).

HOW SUPPLIED

4 times daily for up to 3 days.

One or two drops of Diclofenac Sodium Ophthalmic should be applied to the affected eye within the hour prior to corneal refractive surgery.

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. Laceration complaints were reported in approximately 30% of cases undergoing incisional refractive surgery. The following adverse reactions were reported in approximately 10% or less of the patients: abdominal pain, asthma, chills, dizziness, facial edema, fever, headache, insomnia, 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 their seriousness, frequency of reporting, possible causal connection to topical Diclofenac Sodium Ophthalmic Solution, 0.1%, or a combination of these factors, cannot be made. The reactions, which have been chosen for inclusion due to their seriousness, frequency of reporting, possible causal connection to topical Diclofenac Sodium Ophthalmic Solution, 0.1%, or a combination of these factors, cannot be made. The reactions, which have been chosen for inclusion due to their seriousness, frequency of reporting, possible causal connection to topical Diclofenac Sodium Ophthalmic Solution, 0.1%, or a combination of these factors, cannot be made.

Systemic

The following adverse reactions were reported in 3% 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.

To report SUSPECTED ADVERSE REACTIONS, contact Bausch + Lomb, a division of Valeant Pharmaceuticals North America LLC, at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE

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

DOSE 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 postoperative period.

Conjunctival Surgery

One or two drops of Diclofenac Sodium Ophthalmic should be applied to the operative eye within the hour prior to conjunctival 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 and a gray cap. The 2.5 mL fill and the 5 mL fill are supplied in a 7.5 mL size bottle.

Store at 20°-25°C (68°-77°F). PROTECT FROM LIGHT.

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