HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use KETOROLAC TROMETHAMINE OPHTHALMIC SOLUTION safely and effectively. See full prescribing information for KETOROLAC TROMETHAMINE OPHTHALMIC SOLUTION 0.5%.

INDICATIONS AND USAGE
Ketorolac tromethamine ophthalmic solution is a nonsteroidal, anti-inflammatory indicated for:

- The treatment of inflammation following cataract surgery. (1)
- The temporary relief of ocular itching due to seasonal allergic conjunctivitis. (1)

DOSAGE AND ADMINISTRATION
One drop of Ketorolac tromethamine ophthalmic solution should be applied to the affected eye(s) four times a day for relief of ocular itching due to seasonal allergic conjunctivitis. For the treatment of postoperative inflammation in patients who have undergone cataract extraction, one drop of Ketorolac tromethamine ophthalmic solution should be applied to the affected eye four times daily beginning 24 hours after cataract surgery and continuing through the first 2 weeks of the postoperative period. (2.1)

DOSAGE FORMS AND STRENGTHS
Ophthalmic solution containing 5 mg/mL ketorolac tromethamine. (3)

- 8 mL size bottle filled with 5 mL of solution
- 10 mL size bottle filled with 10 mL of solution

CONTRAINDICATIONS
Hypersensitivity to any component of this product. (4)

WARNINGS AND PRECAUTIONS

- Delayed healing (5.1)
- Cross-sensitivity or hypersensitivity (5.2)
- Increased bleeding time due to interference with thrombocyte aggregation (5.3)
- Corneal effects including keratitis (5.4)

ADVERSE REACTIONS
The most frequent adverse reactions reported by up to 40% of patients participating in clinical trials have been transient stinging and burning on instillation. (6.1)
To report SUSPECTED ADVERSE REACTIONS, contact Sandoz Inc., at 1-800-525-8747 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 10/2017

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1 INDICATIONS AND USAGE

Ketorolac tromethamine ophthalmic solution, 0.5%, is indicated for the temporary relief of ocular itching due to seasonal allergic conjunctivitis. Ketorolac tromethamine ophthalmic solution, 0.5% is also indicated for the treatment of postoperative inflammation in patients who have undergone cataract extraction.

2 DOSAGE AND ADMINISTRATION

The recommended dose of ketorolac tromethamine ophthalmic solution, 0.5%, is one drop (0.25 mg) four times a day for relief of ocular itching due to seasonal allergic conjunctivitis.

For the treatment of postoperative inflammation in patients who have undergone cataract extraction, one drop of ketorolac tromethamine ophthalmic solution, 0.5%, should be applied to the affected eye(s) four times daily beginning 24 hours after cataract surgery and continuing through the first 2 weeks of the postoperative period.

Ketorolac tromethamine ophthalmic solution, 0.5% has been safely administered in conjunction with other ophthalmic medications such as antibiotics, beta blockers, carbonic anhydrase inhibitors, cycloplegics, and mydriatics.

2.1 Recommended Dosing

Patient Dosing

The recommended dose of Ketorolac tromethamine ophthalmic solution is one drop four times a day to the affected eye(s) for relief of ocular itching due to seasonal allergic conjunctivitis.

For the treatment of postoperative inflammation in patients who have undergone cataract extraction, one drop of Ketorolac tromethamine ophthalmic solution should be applied to the affected eye four times daily beginning 24 hours after cataract surgery and continuing through the first 2 weeks of the postoperative period.

3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
Ketorolac tromethamine ophthalmic solution, 0.5% is contraindicated in patients with previously demonstrated hypersensitivity to any of the ingredients in the formulation.

5 WARNINGS AND PRECAUTIONS

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

6.1 Clinical Studies Experience
The most frequent adverse reactions reported with the use of ketorolac tromethamine ophthalmic solutions have been transient stinging and burning on instillation. These reactions were reported by up to 40% of patients participating in clinical trials.

Other adverse reactions occurring approximately 1 to 10% of the time during treatment with ketorolac tromethamine ophthalmic solutions included allergic reactions, corneal edema, iritis, ocular inflammation, ocular irritation, superficial keratitis, and superficial ocular infections.

Other adverse reactions reported rarely with the use of ketorolac tromethamine ophthalmic solutions included: corneal infiltrates, corneal ulcer, eye dryness, headaches, and visual disturbance (blurry vision).

6.2 Postmarketing Experience
The following adverse reactions have been identified during post-marketing use of ketorolac tromethamine ophthalmic solution 0.5% 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 ketorolac tromethamine ophthalmic solution 0.5% or a combination of these factors, include bronchospasm or exacerbation of asthma, corneal erosion, corneal perforation, corneal thinning, and epithelial breakdown [see Warnings and Precautions (5.2, 5.4)].

8 USE IN SPECIFIC POPULATIONS
Click here to enter Use in Specific Populations

8.1 Pregnancy
Teratogenic Effects: Pregnancy Category C.

Ketorolac tromethamine, administered during organogenesis, was not teratogenic in rabbits or rats at oral doses up to 109 times and 303 times the maximum recommended human topical ophthalmic dose, respectively, on a mg/kg basis assuming 100% absorption in humans and animals. When administered to rats after Day 17 of gestation at oral doses up to 45 times the maximum recommended human topical ophthalmic dose, respectively, on a mg/kg basis, assuming 100% absorption in humans and animals, ketorolac tromethamine resulted in dystocia and increased pup mortality. There are no adequate and well-controlled studies in pregnant women. Ketorolac tromethamine ophthalmic solution, 0.5% 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-inhibiting drugs on the fetal cardiovascular system (closure of the ductus arteriosus), the use of ketorolac tromethamine ophthalmic solution, 0.5% during late pregnancy should be avoided.

8.3 Nursing mothers
Because many drugs are excreted in human milk, caution should be exercised when Ketorolac tromethamine ophthalmic solution is administered to a nursing woman.

8.4 Pediatric Use
Safety and efficacy in pediatric patients below the age of 2 have not been established.

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

11 DESCRIPTION
Ketorolac tromethamine ophthalmic solution, 0.5% is a member of the pyrrolo-pyrrole group of nonsteroidal anti-inflammatory drugs (NSAIDs) for ophthalmic use. Its chemical name is (±)-5-benzoyl-2,3-dihydro-1H-pyrrolizine-1-carboxylic acid compound with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) and has the following structure:

![Chemical Structure of Ketorolac Tromethamine](image)

Ketorolac tromethamine ophthalmic solution, 0.5% is supplied as a sterile isotonic aqueous 0.5% solution, with a pH of 7.4. Ketorolac tromethamine ophthalmic solution, 0.5% is a racemic mixture of R-(+)- and S-(-)- ketorolac tromethamine. Ketorolac tromethamine may exist in three crystal forms. All forms are equally soluble in water. The pKa of ketorolac is 3.5. This white to off-white crystalline substance discolors on prolonged exposure to light. The molecular weight of ketorolac tromethamine is 376.41. The osmolality of ketorolac tromethamine ophthalmic solution, 0.5% is 290 mOsmol/kg.

Each mL of ketorolac tromethamine ophthalmic solution, 0.5% contains: **Active:** ketorolac tromethamine 0.5%. **Inactives:** benzalkonium chloride 0.01%; edetate disodium 0.1%; octoxynol 40; purified water; sodium chloride; hydrochloric acid and/or sodium hydroxide to adjust pH.

12 CLINICAL PHARMACOLOGY
Ketorolac tromethamine is a nonsteroidal anti-inflammatory drug which, when administered
systemically, has demonstrated analgesic, anti-inflammatory, and anti-pyretic activity. The mechanism of its action is thought to be due to its ability to inhibit prostaglandin biosynthesis. Ketorolac tromethamine given systemically does not cause pupil constriction.

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. Prostaglandins also appear to play a role in the miotic response produced during ocular surgery by constricting the iris sphincter independently of cholinergic mechanisms.

Two drops (0.1 mL) of 0.5% ketorolac tromethamine ophthalmic solution, instilled into the eyes of patients 12 hours and 1 hour prior to cataract extraction achieved measurable levels in 8 of 9 patients’ eyes (mean ketorolac concentration 95 ng/mL aqueous humor, range 40 to 170 ng/mL). Ocular administration of ketorolac tromethamine reduces prostaglandin E\textsubscript{2} (PGE\textsubscript{2}) levels in aqueous humor. The mean concentration of PGE\textsubscript{2} was 80 pg/mL in the aqueous humor of eyes receiving vehicle and 28 pg/mL in the eyes receiving ketorolac tromethamine 0.5% ophthalmic solution.

One drop (0.05 mL) of 0.5% ketorolac tromethamine ophthalmic solution, was instilled into one eye and one drop of vehicle into the other eye TID in 26 normal subjects. Only 5 of 26 subjects had a detectable amount of ketorolac in their plasma (range 10.7 to 22.5 ng/mL) at Day 10 during topical ocular treatment. When ketorolac tromethamine 10 mg is administered systemically every 6 hours, peak plasma levels at steady state are around 960 ng/mL.

Two controlled clinical studies showed that ketorolac tromethamine ophthalmic solution, was significantly more effective than its vehicle in relieving ocular itching caused by seasonal allergic conjunctivitis.

Two controlled clinical studies showed that patients treated for two weeks with ketorolac tromethamine ophthalmic solution, were less likely to have measurable signs of inflammation (cell and flare) than patients treated with its vehicle.

Results from clinical studies indicate that ketorolac tromethamine has no significant effect upon intraocular pressure; however, changes in intraocular pressure may occur following cataract surgery.

12.1 Mechanism of Action

Ketorolac tromethamine is a nonsteroidal anti-inflammatory drug which, when administered systemically, has demonstrated analgesic, anti-inflammatory, and anti-pyretic activity. The mechanism of its action is thought to be due to its ability to inhibit prostaglandin biosynthesis.

12.3 Pharmacokinetics

Two drops of 0.5% ketorolac tromethamine ophthalmic solution instilled into the eyes of patients 12 hours and 1 hour prior to cataract extraction achieved a mean ketorolac concentration of 95 ng/mL in the aqueous humor of 8 of 9 eyes tested (range 40 to 170 ng/mL).

One drop of 0.5% ketorolac tromethamine ophthalmic solution was instilled into 1 eye and 1 drop of vehicle into the other eye TID in 26 healthy subjects. Five (5) of 26 subjects had detectable concentrations of ketorolac in their plasma (range 11 to 23 ng/mL) at Day 10 during topical ocular treatment. The range of concentrations following TID dosing of 0.5% ketorolac tromethamine ophthalmic solution are approximately 4 to 8% of the steady state mean minimum plasma concentration observed following four times daily oral administration of 10 mg ketorolac in humans (290 ± 70 ng/mL).

13 NONCLINICAL TOXICOLOGY

Click here to enter Nonclinical Toxicology
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Ketorolac tromethamine was not carcinogenic in either rats given up to 5 mg/kg/day orally for 24 months or in mice given 2 mg/kg/day orally for 18 months. These doses are approximately 125 times and 50 times higher respectively than the maximum recommended human topical ophthalmic daily dose given as QID for itching to affected eyes on a mg/kg basis.

Ketorolac tromethamine was not mutagenic in vitro in the Ames assay or in forward mutation assays. Similarly, it did not result in an in vitro increase in unscheduled DNA synthesis or an in vivo increase in chromosome breakage in mice. However, ketorolac tromethamine did result in an increased incidence in chromosomal aberrations in Chinese hamster ovary cells.

Ketorolac tromethamine did not impair fertility when administered orally to male and female rats at doses up to 9 mg/kg/day and 16 mg/kg/day, respectively. These doses are respectively 225 and 400 times higher than the typical human topical ophthalmic daily dose.

14 CLINICAL STUDIES

Two controlled clinical studies showed that ketorolac tromethamine ophthalmic solution was significantly more effective than its vehicle in relieving ocular itching caused by seasonal allergic conjunctivitis.

Two controlled clinical studies showed that patients treated for two weeks with ketorolac tromethamine ophthalmic solution were less likely to have measurable signs of inflammation (cell and flare) than patients treated with its vehicle.

Results from clinical studies indicate that ketorolac tromethamine has no significant effect upon intraocular pressure; however, changes in intraocular pressure may occur following cataract surgery.

16 HOW SUPPLIED/STORAGE AND HANDLING

Ketorolac tromethamine ophthalmic solution, 0.5% is supplied sterile in a white LDPE plastic DROP-TAINER* bottle, a natural dropper tip and a gray polypropylene cap as follows:

- 5 mL in 8 mL bottle NDC 61314-126-05
- 10 mL in 10 mL bottle NDC 61314-126-10

Storage: Store at room temperature 15°-30°C (59°-86°F) with protection from light.

FOR TOPICAL OPHTHALMIC USE ONLY

*DROP-TAINER is a registered trademark of Alcon Research, Ltd.

9015455-1017

Manufactured by
Alcon Laboratories, Inc.
Fort Worth, Texas 76134 for
Sandoz Inc.
Princeton, NJ 08540
Printed in USA
9015455-1017
Revised: October 2017

17 PATIENT COUNSELING INFORMATION
Ketorolac tromethamine ophthalmic solution, 0.5% should not be administered while wearing contact lenses.

17.1 Slow or Delayed Healing
Patients should be informed of the possibility that slow or delayed healing may occur while using nonsteroidal anti-inflammatory drugs (NSAIDs).

17.2 Avoiding Contamination of the Product
Patients should be instructed to avoid allowing the tip of the bottle to contact the eye or surrounding structures because this could cause the tip to become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

Also, to avoid the potential for cross-contamination, the patient should be advised to use one bottle for each eye following bilateral ocular surgery. The use of the same bottle of topical eye drops for both eyes following bilateral ocular surgery is not recommended.

17.3 Contact Lens Wear
Patients should be advised that Ketorolac tromethamine ophthalmic solution should not be administered while wearing contact lenses.

17.4 Intercurrent Ocular Conditions
Patients should be advised that if they develop an intercurrent ocular condition (e.g., trauma or infection) or have ocular surgery, they should immediately seek their physician's advice concerning the continued use Ketorolac tromethamine ophthalmic solution.

17.5 Concomitant Topical Ocular Therapy
Patients should be advised that if more than one topical ophthalmic medication is being used, the medicines should be administered at least 5 minutes apart.

PACKAGE/LABEL PRINCIPAL DISPLAY PANEL
NDC 61314-126-10
Ketorolac Tromethamine Ophthalmic Solution
0.5%
FOR TOPICAL OPHTHALMIC USE ONLY
Rx only
STERILE
10 mL
Sandoz
Ketorolac Tromethamine Ophthalmic Solution 0.5%  
Rx only  
STERILE 10 mL

FOR TOPICAL OPHTHALMIC USE ONLY.
Each mL contains: Active: ketorolac tromethamine 0.5%. Inactives: benzalkonium chloride 0.01%; edetate disodium 0.1%; octoxynol 40; purified water; sodium chloride; hydrochloric acid and/or sodium hydroxide to adjust pH.

Dosage: One drop four times a day.

Manufactured by Alcon Laboratories, Inc.  
Fort Worth, Texas 76134 for Sandoz Inc.  
Princeton, NJ 08540
## Product Information

**Product Type**
- Human Prescription Drug

**Route of Administration**
- Ophthalmic

**Item Code (Source)**
- NDC: 61314-126

## Active Ingredient/Active Moiety

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## Packaging

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## Marketing Information

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## Labeler
- Sandoz Inc (005387188)

## Registrant
- Sandoz Inc (005387188)

## Establishment

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