

KETOROLAC TROMETHAMINE - ketorolac tromethamine solution/ drops
Aurobindo Pharma Limited

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.

KETOROLAC TROMETHAMINE ophthalmic solution 0.4% for topical ophthalmic use
Initial U.S. Approval: 1991

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

Ketorolac tromethamine ophthalmic solution is a nonsteroidal, anti-inflammatory drug (NSAID) indicated for the reduction of ocular pain and burning/stinging following corneal refractive surgery. (1)

----- **DOSAGE AND ADMINISTRATION** -----

One drop of ketorolac tromethamine ophthalmic solution should be applied in the operated eye 4 times per day as needed for pain and burning/stinging for up to 4 days following corneal refractive surgery. (2.1)

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

Ophthalmic solution containing 4 mg/mL ketorolac tromethamine in a 10 mL size bottle filled with 5 mL of solution. (3)

----- **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 common adverse reactions occurring in 1 to 5% of patients included conjunctival hyperemia, corneal infiltrates, headache, ocular edema and ocular pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Aurobindo Pharma USA, Inc. at 1-866-850-2876 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 12/2019

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Ketorolac tromethamine ophthalmic solution is indicated for the reduction of ocular pain and burning/stinging following corneal refractive surgery.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosing

The recommended dose of ketorolac tromethamine ophthalmic solution is one drop four times a day in the operated eye as needed for pain and burning/stinging for up to 4 days following corneal refractive surgery.

2.2 Use With Other Topical Ophthalmic Medications

Ketorolac tromethamine ophthalmic solution has been safely administered in conjunction with other topical ophthalmic medications such as alpha-agonists, antibiotics, beta-blockers, carbonic anhydrase inhibitors, cycloplegics, and mydriatics. Drops should be administered at least 5 minutes apart.

3 DOSAGE FORMS AND STRENGTHS

10 mL size bottle filled with 5 mL of ketorolac tromethamine ophthalmic solution 0.4% (4 mg/mL).

4 CONTRAINDICATIONS

Ketorolac tromethamine ophthalmic solution is contraindicated in patients with previously demonstrated hypersensitivity to any of the ingredients in the formulation.

5 WARNINGS AND PRECAUTIONS

5.1 Delayed Healing

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.

5.2 Cross-Sensitivity or Hypersensitivity

There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs. There have been reports of bronchospasm or exacerbation of asthma associated with the use of ketorolac tromethamine ophthalmic solution in patients who have either a known hypersensitivity to aspirin/non-steroidal anti-inflammatory drugs or a past medical history of asthma. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

5.3 Increased Bleeding Time

With some NSAIDs, 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.

It is recommended that ketorolac tromethamine ophthalmic solution be used with caution in patients with known bleeding tendencies or who are receiving other medications, which may prolong bleeding time.

5.4 Corneal Effects

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.

Postmarketing 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.

Postmarketing experience with topical NSAIDs also suggests that use more than 1 day prior to surgery or use beyond 14 days post-surgery may increase patient risk for the occurrence and severity of corneal adverse events.

5.5 Contact Lens Wear

Ketorolac tromethamine should not be administered while wearing contact lenses.

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling:

- Delayed Healing [*see Warnings and Precautions (5.1)*]
- Cross-Sensitivity or Hypersensitivity [*see Warnings and Precautions (5.2)*]
- Increased Bleeding Time [*see Warnings and Precautions (5.3)*]
- Corneal Effects [*see Warnings and Precautions (5.4)*]

6.1 Clinical Studies Experience

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 rates in the clinical studies of another drug and may not reflect the rates observed in practice.

The most frequently reported adverse reactions for ketorolac tromethamine ophthalmic solution occurring in approximately 1 to 5% of the overall study population were conjunctival hyperemia, corneal infiltrates, headache, ocular edema, and ocular pain.

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 in 1 to 10% of the time during treatment with other 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 ulcer, eye dryness, and visual disturbance (blurry vision).

6.2 Postmarketing Experience

The following adverse reactions have been identified during postmarketing use of ketorolac tromethamine ophthalmic solutions 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 solutions or a combination of these factors, include bronchospasm or exacerbation of asthma, corneal erosion, corneal perforation, corneal thinning and corneal melt, and epithelial breakdown [see *Warnings and Precautions* (5.2, 5.4)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate or well-controlled studies with ketorolac tromethamine in pregnant women. No evidence of teratogenicity has been observed in rats or rabbits with ketorolac tromethamine at clinically relevant doses.

8.2 Lactation

Risk Summary

It is not known whether ketorolac when given topically is present in human milk. Because many drugs are excreted in human milk, caution should be exercised when ketorolac tromethamine is administered to a nursing woman.

8.4 Pediatric Use

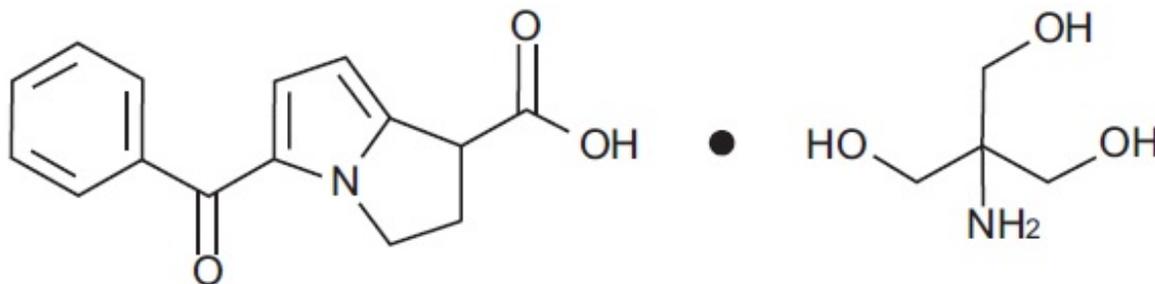
Safety and effectiveness of ketorolac tromethamine in pediatric patients below the age of 3 have not been established.

8.5 Geriatric Use

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

11 DESCRIPTION

Ketorolac tromethamine ophthalmic solution 0.4% 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-1*H*-pyrrolizine-1-carboxylic acid, compound with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1), and its molecular weight is 376.40. Its molecular formula is C₁₉H₂₄N₂O₆ and it has the following structure:



Ketorolac tromethamine ophthalmic solution is supplied as a sterile, isotonic, clear colorless to slightly yellow aqueous 0.4% solution, with a pH of approximately 7.4. Ketorolac tromethamine ophthalmic solution contains 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 or almost white crystalline powder, melt between 165°C and 170°C, with decomposition. The osmolality of ketorolac tromethamine ophthalmic solution is 290 mOsmol/kg.

Each mL of ketorolac tromethamine ophthalmic solution contains: **Active:** ketorolac tromethamine USP 0.4%. **Preservative:** benzalkonium chloride 0.006%. **Inactives:** edetate disodium 0.015%; octoxynol 40; water for injection; sodium chloride; and hydrochloric acid and/or sodium hydroxide to adjust pH.

12 CLINICAL PHARMACOLOGY

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

One drop of 0.5% ketorolac tromethamine ophthalmic solution was instilled into one eye and one drop of vehicle into the other eye TID in 26 healthy subjects. Five of 26 subjects had detectable concentrations of ketorolac in their plasma (range 11 to 23 ng/mL) at day 10 during topical ocular treatment.

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).

14 CLINICAL STUDIES

In two double-masked, multi-centered, parallel-group studies, 313 patients who had undergone photorefractive keratectomy received ketorolac tromethamine ophthalmic solution 0.4% or its vehicle QID for up to 4 days. Significant differences favored ketorolac tromethamine for the reduction of ocular pain and burning/stinging following photorefractive keratectomy surgery.

Results from clinical studies indicate that ketorolac tromethamine has no significant effect upon intraocular pressure.

The safety and effectiveness of ketorolac tromethamine in post-cataract surgery patients has not been established.

16 HOW SUPPLIED/STORAGE AND HANDLING

Ketorolac tromethamine ophthalmic solution 0.4% is a clear colorless to slightly yellow solution supplied in white opaque LDPE container with LDPE nozzle and gray color HDPE cap as follows:

5 mL in 10 mL bottle

NDC 65862-775-05

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

17 PATIENT COUNSELING INFORMATION

Slow or Delayed Healing

Inform patients of the possibility that slow or delayed healing may occur while using nonsteroidal anti-inflammatory drugs (NSAIDs).

Avoiding Contamination of the Product

Instruct patients 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.

Contact Lens Wear

Advise patients that ketorolac tromethamine ophthalmic solution should not be administered while wearing contact lenses.

Intercurrent Ocular Conditions

Advise patients 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 of ketorolac tromethamine.

Concomitant Topical Ocular Therapy

Advise patients that if more than one topical ophthalmic medication is being used, the medicines should be administered at least 5 minutes apart.

Distributed by:

Aurobindo Pharma USA, Inc.
279 Princeton-Hightstown Road
East Windsor, NJ 08520

Manufactured by:

Aurobindo Pharma Limited
Hyderabad - 500038
India

PACKAGE LABEL-PRINCIPAL DISPLAY PANEL - 0.4% - Container Label

NDC 65862-775-05

**Ketorolac
Tromethamine
Ophthalmic Solution
0.4%
For Use in the Eyes Only
Rx only Aurobindo**



N 3 6 5 8 6 2 7 7 5 0 5 4

NDC 65862-775-05
**Ketorolac
Tromethamine
Ophthalmic Solution**
0.4%
For Use in the Eyes Only

Rx only  AUROBINDO

**5 mL
Sterile**
Protect from light.
Code: TS/DRUGS/13/2010

Distributed by:
Aurobindo Pharma USA, Inc.
East Windsor, NJ 08520
Made in India

P1424205

Batch:
Expiry:

PACKAGE LABEL-PRINCIPAL DISPLAY PANEL - 0.4% - Container-Carton

**NDC 65862-775-05
Ketorolac
Tromethamine
Ophthalmic
Solution
0.4%
For Use in the Eyes Only
5 mL
Rx only
AUROBINDO**



KETOROLAC TROMETHAMINE

ketorolac tromethamine solution/ drops

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:65862-775
Route of Administration	OPHTHALMIC		

Active Ingredient/Active Moiety

Ingredient Name		Basis of Strength	Strength	
KETOROLAC TROMETHAMINE (UNII: 4EVE5946BQ) (KETOROLAC - UNII:YZI5105V0L)		KETOROLAC TROMETHAMINE	4 mg in 1 mL	
Inactive Ingredients				
Ingredient Name			Strength	
BENZALKONIUM CHLORIDE (UNII: F5UM2KM3W7)				
EDETATE DISODIUM (UNII: 7FLD91C86K)				
OCTOXYNOL-40 (UNII: 9T1C662FKS)				
WATER (UNII: 059QF0K00R)				
SODIUM CHLORIDE (UNII: 451W47IQ8X)				
HYDROCHLORIC ACID (UNII: QTT17582CB)				
SODIUM HYDROXIDE (UNII: 55X04QC32I)				
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:65862-775-05	1 in 1 CARTON	11/15/2018	
1		5 mL in 1 BOTTLE; Type 0: Not a Combination Product		
Marketing Information				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date	
ANDA	ANDA205191	11/15/2018		

Labeler - Aurobindo Pharma Limited (650082092)

Establishment

Name	Address	ID/FEI	Business Operations
Aurobindo Pharma Limited		650498244	ANALYSIS(65862-775) , MANUFACTURE(65862-775)

Revised: 12/2019

Aurobindo Pharma Limited