

Name of Medicine

ACULAR[®] EYE DROPS

Ketorolac trometamol 5 mg/mL

Composition

Active: ketorolac trometamol 5 mg/mL

Inactive: benzalkonium chloride 0.01% (w/v), disodium edetate 0.1% (w/v), octoxinol 40, sodium chloride, hydrochloric acid and sodium hydroxide (to adjust pH) and purified water.

Description

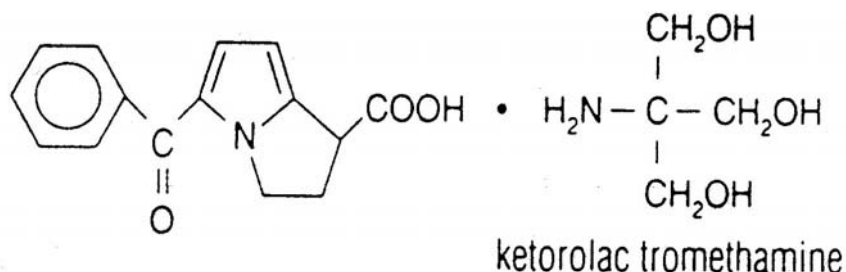
Chemical Name: (±)-5-Benzoyl-2,3-dihydro-1H-pyrrolizine-1-carboxylic acid compound with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1)

Empirical Formula: C₁₉H₂₄N₂O₆ Molecular Weight: 376.41

CAS No: 74103-07-4 pKa: 3.54

Ketorolac trometamol is a white to off-white crystalline substance, which is a racemic mixture. It may exist in three crystalline forms, all of which are equally soluble in water. Ketorolac trometamol 5mg/mL ophthalmic solution is a clear, colourless to pale yellow, sterile, isotonic aqueous solution.

Chemical Structure



Uses

Actions

Ketorolac trometamol is a member of the pyrrolo-pyrrole group of non-steroidal anti-inflammatory drugs for ophthalmic use.

Pharmacology

Ketorolac trometamol is a nonsteroidal, anti-inflammatory agent demonstrating analgesic and anti-inflammatory activity. It is believed to inhibit the cyclo-oxygenase enzyme essential for prostaglandin biosynthesis. Ocular administration of ketorolac trometamol reduces prostaglandin E₂ levels in the aqueous humour. Ketorolac trometamol given systemically does not cause pupil constriction. Results from clinical studies indicate that ACULAR[®] eye drops have no significant effect upon intraocular pressure.

Pharmacokinetics

Two drops (0.1 mL) of 0.5% ACULAR[®] eye drops 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 concentrations 95 nanograms/mL aqueous humour, range 40-170 nanograms/mL). One drop (0.05 mL) of 0.5% ketorolac trometamol solution was instilled into one eye and one drop of the vehicle into the other eye three times a day for 21 days in 26 normal subjects. Only 5 of 26 subjects had detectable amounts of ketorolac in their plasma (range 10.7 to 22.5 nanograms/mL) at Day 10 during topical ocular treatment. When ketorolac is given systemically to relieve pain, plasma levels following chronic systemic use average around 860 nanograms/mL.

Indications

ACULAR[®] eye drops are indicated for the short term (2 - 4 weeks) prophylaxis and reduction in inflammation in patients undergoing cataract extraction.

ACULAR[®] eye drops are also indicated for the short term (2 - 4 weeks) relief of symptoms of seasonal allergic conjunctivitis.

Contraindications

ACULAR[®] eye drops are contraindicated in patients hypersensitive to any of the components of the medication.

The potential exists for cross sensitivity to acetylsalicylic acid and other nonsteroidal anti-inflammatory medicines. ACULAR[®] is contraindicated in patients who have previously exhibited sensitivities to these drugs.

ACULAR[®] eye drops are contraindicated in children.

Warnings and Precautions

Patients with bleeding tendencies:

With some nonsteroidal anti-inflammatory drugs a potential exists 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. ACULAR[®] eye drops should be used with care in patients with known bleeding tendencies, or in patients who are receiving other medications which may prolong bleeding time, or patients with a known history of peptic ulceration.

Bronchospasm: There have been post-marketing reports of bronchospasm or exacerbation of asthma in patients, who have either a known hypersensitivity to aspirin/non-steroidal anti-inflammatory drugs or a past medical history of asthma associated with the use of ACULAR[®], which may be contributory. Caution is recommended in the use of ACULAR[®] of in these individuals.

Delayed Healing: All topical nonsteroidal anti-inflammatory drugs (NSAIDs) may slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.

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.

Topical NSAIDs should be used with caution in 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 as they may be at increased risk for corneal adverse events which may become sight threatening.

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.

Ability to drive:

As ACULAR[®] eye drops may cause transient blurring on instillation, caution is required with the use of hazardous machinery or driving, which are not recommended unless vision is clear.

Masking of infections:

In common with other anti-inflammatory drugs, ACULAR[®] may mask the usual signs of infections.

Soft (hydrophobic) contact lens:

ACULAR[®] eye drops contains benzalkonium chloride as a preservative, and should not be used in patients continuing to wear soft (hydrophobic) contact lens.

Use in Pregnancy and Lactation:

Ketorolac trometamol and its metabolites have been shown to pass into the foetus and milk of animals, and have been detected in human breast milk. Safety in human pregnancy has not been established. Not recommended in pregnancy or lactation. ACULAR[®] should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

An 18-month study in mice at oral doses of ketorolac trometamol equal to the parental Maximum Recommended Human Dose (MRHD) and a 24-month study in rats at oral doses 2.5 times the parental MRHD showed no evidence of tumours. Ketorolac trometamol was not mutagenic in the Ames test, unscheduled DNA synthesis and repair, and in forward mutation assays. Ketorolac did not cause chromosome breakage in the *in vivo* mouse micronucleus assay. At 1590 micrograms/mL approximately 1000 times the average human plasma levels, and at higher concentrations, ketorolac trometamol increased the incidence of chromosomal aberrations in Chinese hamster ovarian cells. Impairment of fertility did not occur in male or female rats at oral doses of 9 mg/kg (53.1 mg/square m) and 16 mg/kg (94.9 mg/square m) respectively.

Adverse Effects

In controlled clinical studies, the most frequently reported adverse events with the use of ACULAR® eye drops have been transient stinging and burning on instillation (eye pain). These events were reported by up to 40% of subjects treated with ACULAR®. Other adverse events reported in controlled clinical studies (at an incidence of >1%) included conjunctivitis (scratching, foreign body sensation, itching, erythema), local allergic reactions, superficial keratitis, corneal oedema, eye infection, eye inflammation, eye irritation and hypersensitivity. Ptosis, blepharitis, photophobia, blurred vision, eye dryness, corneal lesion, iritis, and glaucoma were also reported in >1% of patients in some studies. Uncommon (>0.1% and < 1%) adverse events reported were eye dryness, corneal infiltrates, ulcerative keratitis, visual disturbance and headaches.

There have been post-marketing reports of bronchospasm or exacerbation of asthma in patients who have either a known hypersensitivity to aspirin/non-steroidal anti-inflammatory drugs or a past medical history of asthma, associated with the use of ACULAR® which may be contributory.

Interactions

ACULAR® eye drops have been safely administered with systemic and ophthalmic medications such as antibiotics, sedatives, beta blockers, carbonic anhydrase inhibitors, miotics, mydriatics, cycloplegics, local anaesthetics, and corticosteroids.

Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.

Overdosage

There is no experience of overdosage by the ophthalmic route. If accidentally ingested, fluids should be taken to dilute the effects, if any.

Dosage and Administration

ADULTS:

Seasonal allergic conjunctivitis:

The recommended dose of ACULAR® eye drops for allergic conjunctivitis is one drop (0.25 mg) instilled in the eye four times daily. Treatment may be continued for up to four weeks.

Post operative inflammation

The recommended dose of ACULAR® eye drops for the prophylaxis and treatment of post operative inflammation in patients who have undergone cataract extraction is 1 - 2 drops (0.25 to 0.5 mg) four times daily, starting 24 hours before surgery and continuing for 2 - 4 weeks.

Pharmaceutical Precautions

Discard any unused contents 28 days after opening the bottle.

Package Quantities

5, and 10 mL pack sizes in bottles with dropper applicators.
Store below 25 degrees C and protect from light.

Medicine Classification

Prescription Only Medicine

Name and Address

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Mangere
AUCKLAND

Toll free telephone: 0800 659 912

Date of Preparation

26 August 2011

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