NEW ZEALAND DATA SHEET

1 PRODUCT NAME

ACULAR® (Ketorolac trometamol) 5 mg/mL Eye Drops

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

ACULAR® contains ketorolac trometamol (5 mg/mL) as the active ingredient.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

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.

4 CLINICAL PARTICULARS

4.1 Therapeutic 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.

4.2 Dose and method of administration

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.

4.3 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, phenylacetic acid derivatives, 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.

4.4 Special warnings and precautions for use

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.

Cross-sensitivity

There exists 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.

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.

Information for Patients

ACULAR® contains the preservative benzalkonium chloride, which may be absorbed and cause discoloration to soft contact lenses. Contact lenses should be removed prior to administration of ACULAR® and may be reinserted 15 minutes following administration.

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures to avoid injury and contamination of eye drop.

Masking of infections

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

Eye Injury and Contamination

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures to avoid injury and contamination of eye drops.

Use in the elderly

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

Paediatric population

The safety and efficacy of ACULAR® in pediatric patients below the age of 3 years have not been established.

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.

4.5 Interaction with other medicines and other forms of interaction

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 (see section 4.4. Special warnings and precautions for use)

4.6 Fertility, pregnancy and lactation

Effect on Fertility

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.

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.

4.7 Effects on ability to drive and use machines

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. The patient should wait until their vision clears before driving or using machinery.

4.8 Undesirable 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, keratic precipitates (1%), hem retinal (1%), cystoid macular edema (1%), burning eye (1%), pruritus eye (1%), eye trauma (1%), intraocular pressure (2%), 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. (Note: The frequency of 1% only represents 1 patient).

Post-marketing experience

The following adverse reactions have been identified during post-marketing use. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Since marketed, the following adverse reactions have been observed following the use of ACULAR®: Eye irritation, Eyelid oedema, Eye oedema, Ocular hyperaemia, Conjunctival hyperaemia, Eye swelling, Eye pain, Eye pruritus and Ulcerative Keratitis.

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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose

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

For risk assessment and advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiinflammatory agents, non-steroids, ATC code: S01BC

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

Mechanism of action

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 E_2 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.

5.2 Pharmacokinetic properties

Absorption

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.

Distribution

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.

5.3 Preclinical safety data

Carcinogenesis,

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.

Genotoxicity

Ketorolac trometamol was not genotoxic 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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.

6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store below 30 degrees C and protect from light.

6.5 Nature and contents of container

ACULAR® (ketorolac trometamol) eye drops is supplied in white opaque plastic dropper bottles with dropper applicators.

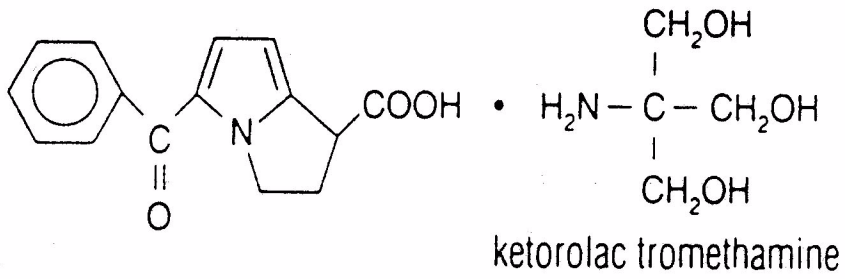
Eye drops: 3 mL, 5 mL and 10 mL (3 mL and 10 mL pack sizes are not marketed).

6.6 Special precautions for disposal

Discard any unused contents 28 days after opening the bottle.

6.7 Physicochemical properties

Chemical structure



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

Empirical Formula: $C_{19}H_{24}N_2O_6$
Molecular Weight: 376.41
pKa: 3.54

CAS No: 74103-07-4

7 MEDICINE SCHEDULE

Prescription Only Medicine

8 SPONSOR

AbbVie Limited
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Wellington, 6011
NEW ZEALAND
PH: 0800 900 030

9 DATE OF FIRST APPROVAL

08 July 1999

10 DATE OF REVISION OF THE TEXT

13 November 2025

Summary table of changes

Section Changed	Summary of new information
6.4	Update to Storage Temperature.
4.8	Updated suspected adverse reactions web address