Professional Information

SCHEDULING STATUS S3

1. NAME OF THE MEDICINE

ACULAR 0,4 % m/v eye drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ketorolac tromethamine 4 mg/ml

Excipient with known effect

Contains benzalkonium chloride 0,006 % m/v

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Eye drops, solution

Clear, colourless to pale yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ACULAR 0,4 % ophthalmic solution is indicated for the reduction of ocular pain and burning/stinging following corneal refractive surgery.

4.2 Posology and method of administration

Posology

The recommended dose is one drop four times a day in the operated eye. It can be instilled for up to 4 days following corneal refractive surgery.

Special populations

Elderly

No dosage adjustment is required for elderly patients.

Paediatric population

Safety and efficacy of ACULAR 0,4 % in children have not been established.

Method of administration

Avoid touching the dropper tip against the eye or any other surface (see section 4.4).

ACULAR 0,4 % ophthalmic solution should not be administered while wearing contact lenses (see section 4.4).

4.3 Contraindications

ACULAR 0,4 % ophthalmic solution is contraindicated in patients with previously demonstrated hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Safety and efficacy in pregnancy and lactation have not been established (see section 4.6).

4.4 Special warnings and precautions for use

There is a potential for cross-sensitivity to acetylsalicylic acid, phenylacetic derivatives and other non-steroidal anti-inflammatory drugs (NSAIDs). There have been reports of bronchospasm or exacerbation of asthma associated with the use of ketorolac tromethamine

0,5 % ophthalmic solution in patients who have either a known hypersensitivity to aspirin or NSAIDs, or a past medical history of asthma. Caution should be exercised when treating patients who have previously exhibited sensitivities to these medicines.

Use of ACULAR 0,4 %, may result in keratitis in susceptible patients. Continued use of ACULAR 0,4 % may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or corneal perforation. These events may lead to blindness.

Patients with evidence of corneal epithelial breakdown should immediately discontinue use of ACULAR 0,4 % and should be closely monitored for corneal health.

There is a risk of increased bleeding time due to interference with thrombocyte aggregation. There have been reports that ocularly-applied non-steroidal anti-inflammatory medicine, like ACULAR 0,4 %, may cause increased bleeding of ocular tissue (including hyphaemas) in conjunction with ocular surgery.

ACULAR 0,4 % should be used with caution in patients with known bleeding tendencies or who are receiving other medicines which may prolong bleeding time (see section 4.5).

Post-marketing experience with topical NSAIDs such as ACULAR 0,4 % 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 lead to blindness. ACULAR 0,4 % should be used with caution in these patients.

Post-marketing experience with topical NSAIDs such as ACULAR 0,4 % also suggest 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.

As the possibility of adverse effects on the corneal permeability and the danger of disruption of the corneal epithelium with prolonged or repeated usage of benzalkonium chloride preserved ophthalmological preparations such as ACULAR 0,4 % cannot be excluded, regular ophthalmological examination is required. Caution should be exercised in the use of benzalkonium chloride preserved topical medication, like ACULAR 0,4 %, over an extended period in patients with extensive ocular surface disease.

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.

ACULAR 0,4 % should not be administered while wearing contact lenses. ACULAR 0,4 % 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 0,4 % and may be reinserted 15 minutes following administration.

4.5 Interaction with other medicines and other forms of interaction

Medicines containing anticoagulants, coumarin- or indandione-derivative, heparin or platelet aggregation inhibitors may interact with ACULAR 0,4 %. Concurrent use with these medicines may increase the risk of post-operative bleeding.

ACULAR 0,4 % may slow or delay healing.

Topical corticosteroids are known to slow or delay healing.

Concomitant use of ACULAR 0,4 % and topical steroids may therefore increase the potential

for delayed healing problems.

There have been no reports of interactions of ketorolac tromethamine ophthalmic solution 0,5 % with topical or injectable medicines used in ophthalmology, used pre-, intra-, or post-operatively, including:

- antibiotics (e.g gentamicin, tobramycin, neomycin, polymyxin),
- sedatives (e.g diazepam, hydroxyzine, lorazepam, promethazine HCl),
- miotics, mydriatics, cycloplegics (e.g acetylcholine, atropine, epinephrine, physostigmine, phenylephrine, timolol maleate),
- hyaluronidase,
- local anaesthetics (e.g bupivacaine HCl, cyclopentolate HCl, lidocaine HCl, tetracaine), or
- corticosteroids.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety in pregnancy and lactation has not been established.

Because of the known effects of NSAIDs on the foetal cardiovascular system of rats (delayed closure of the ductus arteriosus), ACULAR 0,4 % should not be used during pregnancy (see section 4.3).

There are no adequate and well-controlled studies in pregnant women. ACULAR 0,4 % should therefore not be administered in pregnant women

Breastfeeding

It is not known whether ketorolac tromethamine is excreted in human milk following

administration of ACULAR 0,4 %. Therefore, mothers using ACULAR 0,4 % should not breastfeed their infants (see section 4.3).

4.7 Effects on ability to drive and use machines

Transient blurring of vision may occur at instillation. The patient should wait until their vision clears before driving or using machinery.

4.8 Undesirable effects

Tabulated list of adverse reactions

The frequency of adverse reactions documented during clinical trials and through post-marketing experience is given below and is defined as follows: Very Common (≥ 1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000); Very Rare (<1/10,000); Not Known (cannot be estimated from available data).

System organ class	Frequency	Adverse Reaction / Side Effect
Eye disorders	Very common	Stinging or burning on instillation
	Common	Conjunctival hyperaemia, corneal infiltrates, ocular oedema, ocular pain, iritis, ocular inflammation, corneal oedema, ocular irritation, superficial keratitis and superficial ocular infections
	Unknown	Corneal erosion, corneal perforation, corneal thinning, epithelial breakdown, ulcerative keratitis, eye swelling, eyelid oedema and ocular hyperaemia
Nervous system	Common	Headache

disorders		
Skin and subcutaneous tissue disorders	Common	Allergic reactions (itching, rash, redness or swelling of skin)

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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

See section 4.8.

In the event of topical overdose, wash the eye with water. If accidentally ingested, drink fluids to dilute. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A 15.4. Ophthalmic preparations. Other.

Ketorolac tromethamine is a non-steroidal anti-inflammatory drug (NSAID) with analgesic and anti-inflammatory activity. It is believed to inhibit prostaglandin biosynthesis. Results from clinical studies indicate that ketorolac tromethamine has no significant effect upon intraocular pressure.

5.2 Pharmacokinetic properties

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 3 times a day in 26 normal adult subjects. Five 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride

Sodium chloride

Edetate disodium

Octoxynol 40

Sodium hydroxide or hydrochloric acid (for pH adjustment)

Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

18 months

Do not use more than 30 days after first opening

6.4 Special precautions for storage

Store at or below 25 ºC. Do not refrigerate or freeze. Keep container tightly closed.

6.5 Nature and contents of container

Opaque white, low-density polyethylene (LDPE) bottle with a white controlled dropper tip and a grey high impact polystyrene (HIPS) cap. The pack size is a carton containing 1 bottle of 5 ml solution in a 10 ml bottle.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

AbbVie (Pty) Ltd

Building 7, Waterfall Corporate Campus

74 Waterfall Drive

Waterfall City

Midrand, 1685

South Africa

8. REGISTRATION NUMBER

A40/15.4/0282

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17 April 2009

10. DATE OF REVISION OF TEXT

Date of registration:14 April 2021

Date of revision of the most recently revised Professional Information as approved by SAHPRA: 21 April 2023

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