SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

Ketorolac Drops Pharma-Q, 0,5 % Eye drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ketorolac Drops Pharma-Q contains ketorolac trometamol 5 mg/ mL.

Preservatives:

Benzalkonium chloride 0,01 % *m/v*

Disodium edetate 0,1 % *m/v*

Sugar free.

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Eye drops, solution.

Clear, colourless to pale yellow solution practically free from particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Ketorolac Drops Pharma-Q is indicated for the relief of inflammation following ocular surgery.

4.2 Posology and method of administration

Posology

One drop instilled into the eye three times daily starting 24 hours before surgery and continuing post-operatively.

Special populations

Paediatric Population:

The safety and efficacy of Ketorolac Drops Pharma-Q in children have not been established (see section 4.3).

Method of administration

Ophthalmic use.

Instil one drop of the solution into the inferior conjunctival sac of the eye to be treated, while pulling the lower eyelid gently downwards and looking upwards. If used with other eye drops there must be an interval of 5 minutes between applications.

4.3 Contraindications

- Known hypersensitivity to ketorolac trometamol or to any of the excipients listed in section 6.1.
- The potential exists for cross-sensitivity to acetylsalicylic acid and other non-steroidal anti-inflammatory medicines.
- Ketorolac Drops Pharma-Q is contraindicated in individuals who have previously exhibited sensitivities to these medicines.
- Safety and effectiveness in children have not been established.
- Safety of use in pregnant women has not been established (see section 4.6).
- Ketorolac Drops Pharma-Q is not recommended for nursing mothers. Ketorolac trometamol is secreted in human milk after systemic administration (see section 4.6).
- Ketorolac Drops Pharma-Q should not be used while wearing soft contact lenses.

4.4 Special warnings and precautions for use

Benzalkonium chloride

Ketorolac Drops Pharma-Q contains the preservative benzalkonium chloride, which may be absorbed by soft contact lenses. Contact lenses should be removed prior to instillation of Ketorolac Drops Pharma-Q and may be reinserted 15 minutes following administration. Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. Ketorolac Drops Pharma-Q should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be

monitored in case of prolonged use.

As the possibility of adverse effects on the corneal permeability and danger of disruption of the corneal epithelium with prolonged or repeated usage of benzalkonium chloride preserved preparations cannot be excluded, regular ophthalmological examination is required.

Caution should be exercised in the use of benzalkonium chloride preserved topical medication over an extended period in patients with extensive ocular surface disease.

Asthma patients with hypersensitivity to aspirin/NSAIDs

There have been post-marketing reports of bronchospasm or exacerbation of asthma in patients, who have either a known hypersensitivity to aspirin/NSAIDS or a past medical history of asthma associated with the use of Ketorolac 0,5 %, which may be contributory (see section 4.8).

Risk of bleeding

With Ketorolac Drops Pharma-Q, there exists the potential for increased bleeding time due to interference with thrombocyte aggregation. There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphaemas) in conjunction with surgery.

It is recommended that Ketorolac Drops Pharma-Q be used with caution in patients with known bleeding tendencies or who are receiving other medicines which may prolong bleeding time and in patients with known history of peptic ulceration.

Infections

In common with other anti-inflammatory medicines, Ketorolac Drops Pharma-Q may mask the usual signs of infection.

General: Ketorolac Drops Pharma-Q may slow or delay healing.

Keratitis

Use of Ketorolac Drops Pharma-Q may result in keratitis (see section 4.8). In such patients continued use of Ketorolac Drops Pharma-Q 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 Ketorolac Drops Pharma-Q and should be closely monitored for corneal health.

Corneal Adverse Events

Ketorolac Drops Pharma-Q 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 (see section 4.8).

Post-marketing experience with topical NSAIDs, such as Ketorolac Drops Pharma-Q, 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.
Ketorolac drops may cause the risk of anastomotic leakage.

4.5 Interactions with other medicines and other forms of interaction

Ketorolac Drops Pharma-Q has been safely administered with systemic and ophthalmic medicines such as antibiotics, sedatives, beta-blockers, carbonic anhydrase inhibitors, miotics, mydriatics, local anaesthetics and cycloplegics.

Ketorolac Drops Pharma-Q may slow or delay healing. Topical corticosteroids are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical corticosteroids may increase the potential for healing problems.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety and efficacy in human pregnancy have not been established (see section 4.3).

Breastfeeding

Ketorolac trometamol, the active ingredient in Ketorolac Drops Pharma-Q, is secreted in human milk after systemic administration. Therefore, mothers using Ketorolac Drops Pharma-Q should not be breastfeeding their infants (see section 4.3).

Fertility

There are no adequate data from the use of ketorolac trometamol on fertility in humans.

4.7 Effects on ability to drive and use machines

Upon instillation, patients may experience transient blurred vision which may impair the ability to drive or use machinery. If affected, patients should not drive or use machinery until their vision has cleared.

4.8 Undesirable effects

a. Summary of the safety profile

The most frequent adverse events reported with the use of Ketorolac Drops Pharma-Q are transient stinging and burning on instillation.

b. Tabulated summary of adverse reactions

MedDRA system organ class	**Frequency**	**Adverse reactions**
Immune system disorders	Frequent	Hypersensitivity including localised allergic reactions.
Nervous system disorders	Frequent	Headache.

Eye disorders	Frequent	Eye irritation (including burning sensation), eye pain (including stinging), superficial (punctate) keratitis, eye and/or eyelid oedema, ocular pruritus, conjunctival hyperaemia, eye infection, eye inflammation, iritis, keratic precipitates, retinal haemorrhage, cystoid macular oedema, eye trauma, increased intraocular pressure, blurred and/or diminished vision.
	Less frequent	Corneal ulcer, corneal infiltrates, eye dryness, epiphora.
	Frequency unknown	Corneal damage, e.g. thinning, erosion, epithelial breakdown and perforation*, ulcerative keratitis, eye swelling, ocular hyperaemia.
Gastrointestinal disorders	Frequency unknown	Anastomotic leakage
Respiratory, thoracic and mediastinal disorders	Frequency unknown	Bronchospasm or exacerbation of asthma**.

*Occasional post marketing reports of corneal damage including corneal thinning, corneal erosion, epithelial breakdown and corneal perforation have been received. These occurred mainly in patients using concomitant topical corticosteroids and/or with predisposing co-morbidity (see section 4.4).

**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 Ketorolac Drops Pharma-Q which may be contributory.

None of the typical adverse reactions reported with the systemic non-steroidal anti-inflammatory medicines (including ketorolac trometamol) have been observed at the doses used in topical ophthalmic therapy.

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

No case of overdose has been reported. Overdose is unlikely to occur via the recommended method of administration. In the event of topical overdosage, rinse the eye with water. If accidentally ingested, drink fluids to dilute.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

15.4 Ophthalmic preparations. Other.

Pharmacotherapeutic group: Anti-inflammatory agents, non-steroids.

ATC code: S01BC 05.

Ketorolac trometamol is a non-steroidal anti-inflammatory medicine demonstrating analgesic and anti-inflammatory activity. It is believed to inhibit the cyclo- oxygenase enzyme essential for biosynthesis of prostaglandins. Ketorolac has been shown to reduce prostaglandin levels in the aqueous humour after topical ophthalmic administration.

Ketorolac trometamol given systemically does not cause pupil constriction. Results from clinical studies indicate that ketorolac has no significant effect on intraocular pressure.

5.2 Pharmacokinetic properties

Studies suggest that the use of ketorolac trometamol by the ophthalmic route in treatment of

ocular disorders results in low systemic absorption.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride

Disodium edetate

Hydrochloric acid, to adjust pH

Octoxynol 40

Sodium chloride

Sodium hydroxide, to adjust pH

Water for injection

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Shelf-life: 24 months

Shelf-life after first opening of the container: 28 days

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

5 mL pack:

5 mL of Ketorolac Drops Pharma-Q solution is filled in a 5 mL 3-piece container: white opaque low-density polyethylene (LDPE) container with white opaque LDPE open nozzle and grey high density polyethylene (HDPE) screw caps.

10 mL pack:

10 mL of Ketorolac Drops Pharma-Q solution is filled in a 10 mL 3-piece container: white opaque low-density polyethylene (LDPE) container with white opaque LDPE open nozzle and grey high-density polyethylene (HDPE) screw caps.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Pharma-Q Holdings (Pty) Ltd

50 Commando Road

Industria West

Johannesburg

2093

8. REGISTRATION NUMBER(S)

47/15.4/0512

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01 February 2022

10. DATE OF REVISION OF THE TEXT

01 February 2024