CLEAN AMENDED PROPOSED PROFESSIONAL INFORMATION LEAFLET: KELOPT

SCHEDULING STATUS **S3**

1. NAME OF THE MEDICINE

Kelopt® 5,0 mg/ml Ophthalmic Solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ketorolac Tromethamine 5,0 mg/ml.

Excipient(s) with known effect: Preservatives: Benzalkonium Chloride 0,01 % *m/v,* Disodium Edetate Dihydrate 0,05 % *m/v*

For full list of excipients, see section 6.1.

3. PHARMACEUTIAL FORM

Ophthalmic solution.

Clear, colourless solution without suspending particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

KELOPT is indicated for the relief of inflammation following ocular surgery.

KELOPT is indicated for use in adults.

4.2 Posology and method of administration

Posology:

The recommended dose is one drop of KELOPT into the affected eye(s) four times daily starting 24 hours before surgery and continuing post-operatively.

Benzalkonium chloride is known to cause eye irritation and discolour soft contact lenses. Patients that wear soft contact lenses should be instructed to remove their lenses prior to using KELOPT and to wait at least 15 minutes before reinserting them (See WARNINGS AND SPECIAL PRECAUTIONS).

Post marketing experience with topical NSAIDs such as KELOPT suggest that use of these medications for more than 24 hours prior to surgery or use beyond 14 days post-surgery may increase the risk for the occurrence and severity of corneal adverse events (See SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Paediatric population:

Safety and effectiveness of KELOPT in children have not been established.

Method of administration:

Ocular use.

4.3 Contraindications

KELOPT is contraindicated in patients who are hypersensitive to ketorolac tromethamine, benzalkonium chloride or any ingredient in the formulation.

There is a potential for cross-sensitivity to aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs). KELOPT is contraindicated in individuals who have previously exhibited sensitivities to these components (See WARNINGS AND SPECIAL PRECAUTIONS).

Pregnancy and lactation.

KELOPT should not be administered while wearing soft (hydrophilic) contact lenses.

4.4 Special warnings and precautions for use

Since there is potential for cross-sensitivity between KELOPT and other NSAIDs [including aspirin (acetylsalicylic acid)], KELOPT should be used with caution in patients in whom asthma, rhinitis or urticaria is precipitated by aspirin or other NSAIDs.

KELOPT may mask the usual signs of infection.

KELOPT has the potential to increase bleeding time due to interference with thrombocyte aggregation and may cause increased bleeding of ocular tissue (including hyphemas) in conjunction with ocular surgery.

KELOPT should be used with caution in patients with a known history of peptic ulceration, in patients who have bleeding tendencies or who are receiving other medication which may prolong the bleeding time.

Keratitis may result from the use of KELOPT. Continued use of KELOPT may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or cornea perforation in some susceptible patients. These events may threaten vision. KELOPT should be immediately

discontinued in patients with evidence of corneal epithelial breakdown and these patients should be closely monitored for corneal health.

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. It is therefore recommended that KELOPT be used with caution in these patients.

The use of KELOPT for 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.

KELOPT may slow or delay the healing process.

Benzalkonium chloride is known to cause eye irritation and discolour soft contact lenses. Patients that wear soft contact lenses should be instructed to remove their lenses prior to using KELOPT and to wait at least 15 minutes before reinserting them (See DOSAGE AND DIRECTIONS FOR USE).

In view of KELOPT's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.

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 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.

4.5 Interaction with other medicines and other forms of interaction

Concomitant use with medication containing anticoagulants, coumarin- or indandione-derivatives, heparin or platelet aggregation inhibitors may increase the risk of post-operative bleeding.

Since KELOPT and topical corticosteroids slow or delay healing, concomitant use of these agents may increase the potential for healing problems.

KELOPT has been safely administered with systemic and ophthalmic medication such as carbonic anhydrase inhibitors, cycloplegics, beta-blockers, antibiotics, miotics and mydriatrics.

4.6 Fertility, pregnancy and lactation

Pregnancy:

Safety and efficacy of KELOPT in pregnant women have not been established, but due to the known effects of prostaglandin-inhibiting agents on the foetal cardiovascular system of rats (closure of the ductus arteriosus), KELOPT should not be used during pregnancy (See CONTRAINDICATIONS).

Regular use of KELOPT during the third trimester of pregnancy may result in premature closure of the foetal ductus arteriosus in utero, and possibly, in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed and its duration increased.

Lactation:

KELOPT is not recommended for women breastfeeding their infants since ketorolac tromethamine is excreted into human milk following systemic administration (See CONTRAINDICATIONS).

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:

KELOPT may cause transient burning on instillation. Patients should be advised not to drive or use machines unless vision is clear.

4.8 Undesirable effects

Immune system disorders:	
Frequent:	Allergic reactions such as rash, itching, redness or swelling of the skin
Nervous system disorders:	
Frequent:	Headache.
Eye disorders:	
Frequent:	Stinging or burning upon instillation. Minor symptoms of ocular irritation. Superficial ocular infections, corneal infiltrates, superficial keratitis, ocular irritation, conjunctival hyperaemia, ocular inflammation, ocular pain, ocular oedema, iritis, corneal oedema.
Less frequent:	Dry eyes, corneal ulceration.

Frequency unknown:	Blurring/visual disturbances. Corneal perforation, corneal erosion, corneal thinning and epithelial breakdown.

4.9 Overdose

In the event of topical overdosage, flush the eye with water. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A 15.4 Ophthalmic preparations, others.

Ketorolac tromethamine is a non-steroidal anti-inflammatory agent, demonstrating both anti-inflammatory and analgesic activity.

The mechanism of action of ketorolac tromethamine is believed to be due to its ability to inhibit the cyclo-oxygenase enzymes, which are essential for the biosynthesis of certain prostaglandins in the arachidonic acid pathway.

Ketorolac tromethamine has been shown to reduce aqueous humour concentrations of these prostaglandins (PGE_2) following topical application to the eye. Ketorolac tromethamine has no significant effect on intraocular pressure.

Systemic administration of ketorolac tromethamine does not cause pupil constriction.

5.2 Pharmacokinetic properties

Following topical administration of one drop (0,05 ml) of 0,5 % ketorolac tromethamine ophthalmic solution into one eye and one drop of vehicle into the other eye, 3 times a day in 26 normal individuals, it was noted that only some of the individuals had a detectable amount of ketorolac in their plasma (range: 10,7 to 22,5 ng/ml) at day 10. Steady state plasma levels of about 960 ng/ml is achieved when 10 mg of ketorolac tromethamine is administered systemically every 6 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium Phosphate Anhydrous

Monosodium Phosphate Dihydrate

Sodium Chloride

Purified Water

Benzalkonium Chloride

Disodium Edetate Dihydrate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Unopened: 3 years

Do not use more than 28 days after opening.

6.4 Special precautions for storage

Store at or below 30 °C. Protect from light.

Keep the container in the outer carton. Do not refrigerate or freeze.

Discard any unused portion.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

KELOPT ophthalmic solution is supplied in an opaque white sterile dropper bottle with a white sterile capillary plug and white sterile cap, containing 5 ml solution.

6.6 Special precautions for disposal and other handling

No special requirements.

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

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Actor Pharma (Pty) Ltd[1]

Unit 7, Royal Palm Business Estate

646 Washington Street

Halfway House

Midrand, 1685

Gauteng, South Africa

8. REGISTRATION NUMBER

45/15.4/1033

9. DATE OF FIRST AUTHORISATION

25 August 2015

10. DATE OF REVISION OF THE TEXT

12 June 2020

® - KELOPT is a registered trademark of Actor Pharma

[1] Company Registration number: 2008/008787/07

KEL/PI/02/03.2020