SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Voltarol Ophtha Multidose 0.1% Eye Drops

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains diclofenac sodium 1mg/ml

Excipient with known effect: benzalkonium chloride (0.05 mg/ml)
For the full list of excipients, see section 6.1**.**

3 PHARMACEUTICAL FORM

Eye drops solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

i. Inhibition of peroperative miosis during cataract surgery (Voltarol Ophtha Multidose has no intrinsic mydriatic properties and does not replace standard mydriatic agents).

ii. Treatment of post-operative inflammation in cataract surgery.

iii. Control of ocular pain and discomfort associated with corneal epithelial defects after excimer PRK surgery or accidental non-penetrating trauma.

iv. Control of inflammation after Argon Laser Trabeculoplasty (ALT).

v. The relief of the ocular signs and symptoms of Seasonal Allergic Conjunctivitis (SAC).

vi. Treatment of inflammation and discomfort after strabismus surgery

vii. Treatment of ocular pain and discomfort after radial keratotomy

4.2 Posology and method of administration

Voltarol Ophtha eye drop solution is for instillation into the conjunctival sac only. It should never be injected subconjunctivally, nor should it be directly introduced into the anterior chamber of the eye.

Adults:

Prophylaxis of preoperative miosis	Apply 1 drop four times during the 2 hours before surgery.
Control of post-operative inflammation	Apply 1 drop 4 times daily for up to 28 days.
Control of Post-PRK pain and discomfort	Apply 1 drop 2 times in the hour prior to surgery, 1 drop 2 times five minutes apart immediately after PRK surgery and then post-operatively 1 drop every 2-5 hours while awake for up to 24 hours.
Control of ocular pain associated with corneal epithelial defects after accidental non-penetrating trauma.	Apply 1 drop 4 times daily for up to 2 days.
Control of post-ALT inflammation.	Apply one drop 4 times during the 2 hours before ALT, and then one drop 4 times daily for up to 7 days.
The relief of the ocular signs and symptoms of Seasonal Allergic Conjuctivitis.	Apply one drop 4 times daily for as long as required.
Treatment of inflammation and discomfort after strabismus surgery	One drop 4 times daily in the 1st week, thrice daily in the 2nd week, twice daily in the 3rd week and as required in the 4th week
Treatment of ocular pain and discomfort after radial keratotomy.	Pre-operatively one drop before surgery, post-operatively one drop immediately after surgery, and then one drop 4 times daily for up to 2 days.

Paediatric use: Voltarol Ophtha and Voltarol Ophtha SDU are not indicated for use in children. Paediatric experience is limited to a few published clinical studies in strabismus surgery.

Following instillation of the eye drops, nasolacrimal occlusion or closing the eyes for 5 minutes may reduce the systemic absorption. This may result in a decrease in systemic side effects and an increase in local activity.

4.3 Contraindications

Patients with known hypersensitivity to any of the ingredients.

Like other non-steroidal anti-inflammatory agents, Voltarol is also contraindicated in patients in whom attacks of asthma, urticaria or acute rhinitis are precipitated by acetylsalicylic acid or by other drugs with prostaglandin synthetase inhibiting activity. Intraocular use during surgical procedure is also contraindicated.

4.4 Special warnings and precautions for use

The anti-inflammatory activity of ophthalmic non-steroidal anti-inflammatory agents (NSAIDs) may mask the onset and/or progression of ocular infections. In the presence of infection, or if there is a risk of infection, appropriate therapy (e.g. antibiotics) should be given concurrently with Voltarol Ophtha Multidose.

Although there have been no reported adverse events, there is a theoretical possibility that patients receiving other medications which may prolong bleeding time, or with known haemostatic defects may experience exacerbation with Voltarol Ophtha Multidose.

Caution should be exercised when topical NSAIDs such as diclofenac are used concomitantly with topical steroids (see section 4.5 Interaction with other medicinal products and other forms of interaction).

Following instillation of the eye drops, nasolacrimal occlusion or closing the eyes for 3 minutes may reduce the systemic absorption. This may result in a decrease in systemic side effects and an increase in local activity.

This medicine contains 0.0014 mg benzalkonium chloride in each drop, which is equivalent to 0.05 mg/ml.

Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. 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.

Benzalkonium chloride may be absorbed by soft contact lenses and may change the colour of the contact lenses. Patients should be advised to remove contact lenses before using this medicinal product and to wait at least 15 minutes before reinsertion.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of topical NSAIDs such as diclofenac and topical steroids in patients with significant pre-existing corneal inflammation may increase the risk of developing corneal complications, therefore caution should be used.

An interval of at least five minutes between the application of the different medicinal products must be allowed.

4.6 Pregnancy and lactation

Pregnancy
There are no data on the use of Voltarol Ophtha or Voltarol Ophtha Multidose 0.1% in pregnancy. Studies in animals with diclofenac have shown reproductive toxicity (see Section 5.3).

1st and 2nd Trimester: Animal studies have so far shown no risk to the foetus but no controlled studies in pregnant women are available.

3rd Trimester: Voltarol Ophtha should not be used, due to a possible risk of premature closure of the ductus arteriosus and possible inhibition of contractions.

Lactation
Diclofenac is excreted in breast milk. However, at therapeutic doses of Voltarol Ophtha no effects on the suckling child are anticipated. Use of ocular diclofenac is not recommended during breast feeding unless the expected benefits outweigh the possible risks.

4.7 Effects on ability to drive and use machines

Patients with blurred vision should refrain from driving a vehicle or operating machines.

4.8 Undesirable effects

Very frequent: Eye pain.

The other frequently observed adverse reaction is a transient, mild to moderate eye irritation.

Other less frequently observed reactions are eye pruritus, ocular hyperaemia and blurred vision immediately after instillation of the eye drops.

Punctate keratitis or corneal disorders have been observed, usually after frequent application.

In patients with risk factors of corneal disorders such as during the use of corticosteroids or with concomitant diseases such as infections or rheumatoid arthritis, diclofenac has been associated, in rare cases, with ulcerative keratitis, corneal thinning, punctuate keratitis, corneal epithelium defect and corneal oedema, which might become sight-threatening. Most patients were treated for a prolonged period of time.

Allergic conditions have been reported for ocular reactions such as conjunctival hyperaemia, allergic conjunctivitis, eyelid erythema, oedema, and pruritus, and systemic hypersensitivity reactions such as urticaria, rash, eczema, erythema, pruritus, cough and rhinitis.

In rare cases dyspnoea and exacerbation of asthma have been reported.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard

4.9 Overdose

There is practically no risk of adverse effects due to accidental oral ingestion, since a 5ml bottle of the eye drops contains only 5mg of diclofenac sodium, corresponding to about 3% of the recommended maximum daily adult dose of Voltarol after oral administration. By way of comparison, the maximum oral daily dose for diclofenac sodium recommended in children is 2mg/kg body weight.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Voltarol Ophtha Multidose contains diclofenac sodium, a non-steroidal compound with pronounced anti-inflammatory and analgesic properties. Inhibition of prostaglandin biosynthesis, which has been demonstrated experimentally, is regarded as having an important bearing on its mechanism of action. Prostaglandins play a major role in the causation of inflammation and pain.

In clinical trials, Voltarol Ophtha has been found to:

i. inhibit miosis during cataract surgery

ii. reduce inflammation following surgical interventions

iii. reduce ocular pain and discomfort associated with corneal epithelial defects after excimer PRK surgery or accidental non-penetrating trauma.

iv. reduce the incidence of angiographic cystoid macular oedema after cataract surgery but clinical significance remains to be established.

v. reduce ocular inflammation and discomfort more effectively than topical steroids after strabismus surgery whilst avoiding steroidal adverse effects such as delayed conjunctival wound healing and raised intraocular pressure

vi. reduce ocular inflammation, pain and discomfort (photophobia, burning/stinging, foreign body sensation, deep headache-like ocular pain and itching) more effectively than placebo eye drops after corneal incisional surgery such as radial keratotomy.

The effective daily dose after ocular application of Voltarol Ophtha Multidose (approximately 0.25 - 0.5 mg diclofenac sodium) corresponds to less than 1% of the daily dose recommended for Voltarol in rheumatic indications.

Voltarol Ophtha Multidose Eye Drops contain a cyclodextrin, hydroxypropyl γ-cyclodextrin (HPγ-CD). Cyclodextrins (CDs) increase the aqueous solubility of some lipophilic water-insoluble drugs. It is believed that CDs act as true carriers by keeping hydrophobic drug molecules in solution and delivering them to the surface of biological membranes

5.2 Pharmacokinetic properties

In rabbits, peak concentrations of ^{14}C-labelled diclofenac could be demonstrated in the cornea and conjunctiva 30 minutes after application. The highest amounts are found in these two tissues and in the choroid and retina. Elimination was fast and almost complete after 6 hours.

Penetration of diclofenac into the anterior chamber has been confirmed in humans. No measurable levels of diclofenac could be found in humans after ocular application of diclofenac sodium eye drops.

5.3 Preclinical safety data

Preclinical data of systemically applied diclofenac from acute and repeated dose toxicity studies, as well as from genotoxicity and carcinogenicity studies revealed no specific hazard for humans at the intended therapeutic doses.

In reproductive and developmental toxicity studies systemic diclofenac has been shown to cross the placental barrier in mice and rats. Whilst no teratogenic effects have been demonstrated, maternally toxic doses were associated with dystocia, prolonged gestation, decreased foetal survival, and intrauterine growth retardation. The effects of diclofenac on fertility and delivery as well as the constriction of the ductus arteriosus in utero are pharmacological consequences of this class of prostaglandin synthesis inhibitors

Local ocular tolerance and toxicity of Voltarol Ophtha and Voltarol Ophtha Multidose 0.1% eye drops (containing hydroxypropyl-gamma cyclodextrin) were investigated and no evidence of toxicity and local adverse effects was found.

Concentrations of HP-gamma-CD in plasma and aqueous humor were below detection limits (1 nMol/mL) in rabbits after single or four times daily (q.i.d.) ocular administration of Voltarol Ophtha Multidose 0.1% eye drops.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
Disodium edetate
Hydroxypropyl γ-cyclodextrin
Hydrochloric acid
Propylene glycol
Trometamol
Tyloxapol
Water for injections

6.2 Incompatibilities

None known

6.3 Shelf life

Unopened: 24 months
Opened: 4 weeks

6.4 Special precautions for storage

No special precautions for storage.

6.5 Nature and contents of container

5ml white LDPE bottle with LDPE dropper and HDPE closure.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Laboratoires Thea
12, rue Louis-Blériot
63017 Clermont-Ferrand Cedex 2
France

8 MARKETING AUTHORISATION NUMBER(S)

PL 20162/0017

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

22/08/2002 / 26/02/2009

10 DATE OF REVISION OF THE TEXT

11/11/2020