NOVARTIS

## Voltaren® Ophtha

Anti-inflammatory agents, non-steroids.

## COMPOSITION AND PHARMACEUTICAL FORM

Voltaren Ophtha: one mL contains 1 mg of diclofenac sodium.

Eye drops, solution.

For a full list of excipients, see section EXCIPIENTS.

## INDICATIONS

- Post-operative inflammation following cataract surgery and other surgical interventions.
- Preoperative and postoperative prophylaxis of cystoid macular oedema associated with lens extraction and intraocular lens implantation.
- Post-traumatic inflammation in patients with non-penetrating wounds
- Inhibition of miosis during cataract surgery
- Non-infectious inflammatory conditions affecting the anterior region of the eye

## DOSAGE AND ADMINISTRATION

### Adults:

#### Eye surgery and its complications

Preoperative: Instill up to 5 doses of 1 drop each over the course of the 3 hours preceding surgery.

Postoperative: Instill 3 doses of 1 drop each on the day of the operation, followed by 1 drop 3–5 times daily for as long as necessary.

#### Treatment of pain and discomfort, post-traumatic inflammation

One drop 4 to 6 hourly.

**Elderly:** There is no indication that dosage needs to be modified for the elderly.

**Paediatric use:** Voltaren Ophtha is not indicated for use in children. Paediatric experience is limited to a few published clinical studies in strabismus surgery.

The dispenser remains sterile until the original closure is broken. Patients must be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures as this may contaminate the solution.

If more than one medication needs to be instilled in the eye, an interval of at least 5 minutes between application of the different medicinal products must be allowed.

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

Eye drops are not for injection. They should never be injected subconjunctivally, nor should they be directly introduced into the anterior chamber of the eye.

## CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients (see section EXCIPIENTS).

As with other non-steroidal anti-inflammatory agents, Voltaren Ophtha is contraindicated in patients in whom attacks of asthma, urticaria, or acute rhinitis are precipitated by acetylsalicylic acid or by other drugs with prostaglandin synthesis inhibiting activity. There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other non-steroidal anti-inflammatory agents.

## SPECIAL WARNINGS AND PRECAUTIONS FOR USE

The anti-inflammatory activity of ophthalmic NSAIDs including diclofenac may mask the onset and/or progression of ocular infections.

There is a possibility that patients receiving other medications which may prolong bleeding time, or with known hemostatic defects may experience exacerbation with Voltaren Ophtha (See Section INTERACTIONS).

Topical NSAIDs are known to slow or delay healing. Topical ophthalmic corticosteroids may slow corneal wound healing. Caution should be exercised when topical NSAIDs such as diclofenac are used concomitantly with topical steroids (see section INTERACTIONS).

Patients with evidence of corneal epithelial breakdown should immediately discontinue use of Voltaren Ophtha and should be monitored closely for corneal health (See Section UNDESIRABLE EFFECTS).

The wearing of contact lenses is discouraged during treatment of an ocular inflammation. The Voltaren Ophtha formulation contains benzalkonium chloride (BAK) as a preservative which may cause eye irritation and is known to discolour soft contact lenses. Avoid contact with soft contact lenses. However, if the healthcare provider considers contact lenses use appropriate, patients must be instructed to remove contact lenses prior to application of Voltaren Ophtha and wait at least 15 minutes before reinsertion.

## INTERACTIONS

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, such as slow or delayed corneal healing, therefore caution should be used.

Concomitant use of Voltaren Ophtha with medications that prolong bleeding time may increase the risk of hemorrhage. (See section SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

## FERTILITY, PREGNANCY AND LACTATION

### Fertility

Studies have not been performed to evaluate the effect of topical ocular administration of Voltaren Ophtha on human fertility. Animal studies suggest that prostaglandins are necessary for implantation. Therefore, long-term use of NSAIDs by prescription for chronic non-reproductive disorders and continuing use of over-the-counter NSAIDs preparations, while trying to conceive, could potentially adversely affect the peri-implantation process and outcome (See Section PRECLINICAL SAFETY DATA).

### Pregnancy

Animal studies following oral dosing with diclofenac have so far shown no teratogenicity or risk to the foetus during the first and second trimesters of pregnancy.

There have been no adequate, well-controlled studies for the use of Voltaren Ophtha in pregnant women; therefore, its use should be avoided during the third trimester of pregnancy, due to the known effects of prostaglandin biosynthesis inhibition on the fetal cardiovascular system, including the closure of ductus arteriosus (See Section PRECLINICAL SAFETY DATA).

### Lactation

There is insufficient information on the excretion of diclofenac in human milk after the use of Voltaren Ophtha. Following oral administration of 50-mg coated tablets (content of 10, 5 mL bottles of Voltaren Ophtha) only traces of the active substance were detected in breast milk.

Use of ocular diclofenac is not recommended during breast-feeding, unless the expected benefits outweigh the possible risks.

## EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs after application, the patient must wait until the vision clears before driving or using machinery.

## UNDESIRABLE EFFECTS

Tabulated list of adverse reactions [Clinical Studies]

The following adverse reactions have been reported during Alcon clinical studies with Diclofenac Sodium Ophthalmic Solution 0.1% and are classified according to the subsequent convention: 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) and very rare (<1/10,000). Within each frequency-grouping, adverse reactions are presented in order of decreasing seriousness.

**Indication: Treatment of postoperative inflammation in patients who have undergone cataract extraction**

| System organ classification | MedDRA Preferred Term (v.18.1) |
|---|---|
| Immune system disorders | *Uncommon*: hypersensitivity |

| | |
|---|---|
| Eye disorders | *Common*: punctate keratitis, eye pain, eye irritation, eye pruritus, conjunctival hyperaemia<br><br>*Uncommon*: keratitis, intraocular pressure increased, corneal oedema, conjunctival oedema, corneal deposits, conjunctival follicles, ocular discomfort, eye discharge, eyelid margin crusting, lacrimation increased, eyelid irritation, ocular hyperaemia |
| General disorders and administration site conditions | *Uncommon*: impaired healing |

Tabulated list of adverse reactions [Post-Marketing Surveillance]
The following adverse reactions have been identified from post-marketing surveillance following administration of Diclofenac sodium Eye Drops, Solution. Frequency cannot be estimated from the available data. Within each System Organ Class adverse reactions are presented in order of decreasing seriousness.

| **System organ classification** | **Adverse reactions** ***[MedDRA Preferred Term (v.18.1)]*** |
|---|---|
| Infections and infestations | rhinitis |
| Eye disorders | corneal perforation, ulcerative keratitis, corneal epithelium defect, corneal opacity, corneal thinning, allergic conjunctivitis, eye allergy, eyelid erythema, eyelid oedema, eyelid pruritus, vision blurred |
| Respiratory, thoracic and mediastinal disorders | asthma exacerbations, dyspnoea, cough |
| Skin and subcutaneous tissue disorders | urticaria, rash, eczema, erythema, pruritus |

## OVERDOSE

No toxic effects are likely to occur in case of overdose with ocular use, nor in the event of accidental oral ingestion.

## PHARMACODYNAMICS

Pharmacotherapeutic group: anti-inflammatory agents, non-steroids.
ATC code: S01BC03

Diclofenac sodium is one of a series of phenylacetic acids that has demonstrated anti-inflammatory and analgesic properties in pharmacological studies. It is thought to inhibit the enzyme cyclooxygenase, which is essential in the biosynthesis of prostaglandins.

Clinical trials have demonstrated that diclofenac inhibits miosis during cataract surgery and reduces ocular inflammation and pain associated with corneal epithelial defects after some types of surgical intervention.

Voltaren Ophtha contains a cyclodextrin, hydroxypropyl gamma-cyclodextrin (HPgamma-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.

## PHARMACOKINETICS

Ocular pharmacokinetics

In rabbits, peak concentrations of $^{14}C$-labelled diclofenac could be demonstrated in the cornea and conjunctiva 30 minutes after application. Elimination was rapid and almost complete after 6 hours. Ocular inflammation changes diclofenac disposition in the rabbit with decreases in exposure to specific ocular tissues.

Penetration of diclofenac into the anterior chamber was confirmed in humans. Aqueous humor $C_{max}$ value was reported as 82 ng/mL at 2.4 hours after ocular instillation and remained above 20 ng/mL for 4 hours with a mean residence time of 7.4 hours. No measurable plasma levels of diclofenac could be found after ocular application of 0.1% diclofenac over 4 hours.

## PRECLINICAL SAFETY DATA

Non-clinical data revealed no specific hazard for humans based on conventional repeated-dose topical ocular toxicity studies, genotoxicity or carcinogenicity.

Administration of diclofenac to male and female rats at 1000 times the recommended topical human dose did not affect fertility.

Diclofenac and other Non-Steroidal Anti-Inflammatory Drugs (NSAID) are known to inhibit prostaglandins, which play an important role in implantation at the level of both the embryo and the mother. Prostaglandins are necessary for hatching of mouse blastocytes *in vitro* by accumulation of these compounds in the blastocyst fluid. In rats, administration of an NSAID (sodium salicylate) suppressed these changes. Prostaglandins are also necessary for decidualization and can have a significant effect on induced implantations when instilled in the uterine lumen.

Systemic diclofenac has been shown to cross the placental barrier in mice and rats.

Based on human experience, diclofenac, like other NSAIDs, is suspected to cause premature constriction of the ductus arteriosus in utero, in the newborn when administered during the last trimester of pregnancy. At maternally toxic doses of diclofenac, dystocia, prolonged gestation, decreased fetal survival, and intrauterine growth retardation were observed in rat studies. Similar to other NSAIDs, persistent pulmonary hypertension of the newborn may occur if these agents are used in the third trimester of pregnancy.

In mice, rats and rabbits, teratogenicity was not observed up to doses that caused maternal toxicity

## EXCIPIENTS

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

Pharmaceutical formulations may vary between countries.

## INCOMPATIBILITIES

Not applicable.

## STORAGE

See folding box.

Voltaren Ophtha should not be used after the date marked “EXP” on the pack.

## INSTRUCTIONS FOR USE AND HANDLING

***Note***: Voltaren Ophtha must be kept out of the reach and sight of children.

### Manufacturer:

See folding box.

### International Package Leaflet

Information issued: September 2015.SIN

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## Novartis Pharma AG, Basel, Switzerland