**PRESCRIBING INFORMATION**

# VOLTAREN® OPHTHA EYE DROPS

## 1 Name of the medicinal product

Voltaren Ophtha Eye Drops.

## 2 Qualitative and quantitative composition

One mL of Voltaren® Ophtha Eye Drops contains 1 mg of diclofenac sodium.

For a full list of excipients, see section 6.1 List of excipients.

## 3 Pharmaceutical form

Eye drops, solution.

## 4 Clinical particulars

### 4.1 Therapeutic indications

• Post-operative inflammation following cataract extraction.
• Control of ocular pain and discomfort associated with corneal epithelial defects after laser excimer PRK surgery or accidental trauma.

### 4.2 Posology, dosage and method of administration

**Adults**

**a) Ocular surgery and its complications**

Preoperatively, up to 1 drop 5 times during the 3 hours before surgery.
Postoperatively, 1 drop 3 times on the day of surgery, followed by 1 drop 3 to 5 times daily for as long as required.

**b) Treatment of pain and discomfort**

One drop 4 to 6 hourly.

When pain is due to a surgical procedure (e.g. refractive surgery). instill 1 drop, 30-60 minutes prior to surgery, into the eye to be operated on. During the first 10 minutes following surgery, instill 1-2 doses of 1 drop each, followed by 1 drop 4 times daily for 2 days.

**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 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 3 minutes may reduce systemic absorption. This may result in a decrease in systemic side effects and an increase in local activity.

## 4.3 Contraindications

• Known hypersensitivity to the active substance or to any of the excipients (see section 6.1 List of excipients).

• As with other non-steroidal anti-inflammatory agents, Voltaren Ophtha Eye Drops 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.

## 4.4 Special warnings and precautions for use

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

The anti-inflammatory activity of ophthalmic NSAIDs (including diclofenac) may mask the symptoms of infection. In the presence of an infection or if there is a risk of infection, appropriate therapy (e.g. with antibiotics) should be given concurrently with Voltaren Ophtha Eye Drops.

If the symptoms do not respond adequately, the diagnosis should be reconsidered (infection, hypersensitivity to the product).

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 Voltaren Ophtha Eye Drops. During surgery, the product should therefore be used with caution in patients at a heightened risk of bleeding, or in those being treated with an anticoagulant.

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).

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.

Voltaren Ophtha Eye Drops should not be used while wearing soft contact lenses. The lenses must be removed before application of the drops and not reinserted earlier than 15 minutes after use.

Voltaren Ophtha Eye Drops contains benzalkonium chloride as a preservative which may cause eye irritation and is known to discolour soft contact lenses. Voltaren Ophtha Eye Drops should not be used for inhibition of miosis during cataract surgery.

Application of NSAIDs to the eyes can cause keratitis. Prolonged topical use of NSAIDs caused epithelial damage and corneal thinning, erosion, ulceration and perforation in susceptible patients. These effects can result in visual impairment. Treatment should be withdrawn immediately at the first sign of epithelial damage, and the patient should be closely monitored during healing.

## 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 manifest, significant pre-existing corneal inflammation may increase the risk of developing corneal complications, therefore caution should be used.

Ocular diclofenac at 0.1% has been used safely in clinical studies in combination with antibiotics and beta-blocking agents for ocular use.

When using additional ophthalmic preparations, an interval of at least 5 minutes should be observed between each application in order to avoid washing out any of the active substances.

## 4.6 Pregnancy and lactation

### Pregnancy

No reproductive toxicity studies have been conducted with Voltaren Ophtha Eye Drops.

**Preclinical data**: Systemic diclofenac has been shown to cross the placental barrier in mice and rats, but had no influence on the fertility of parent animals in rats. There was no evidence that diclofenac had a teratogenic potential in routine mice, rat or rabbit embryo-foetal development studies. In rats, maternally toxic doses were associated with dystocia, prolonged gestation, decreased foetal survival, and intrauterine growth retardation. The slight effects of diclofenac on fertility and delivery as well as constriction of the ductus arteriosus in utero are pharmacological consequences of this class of prostaglandin synthesis inhibitors.

The prenatal, perinatal and postnatal development of the offspring were not affected. Animal studies have so far shown no risk to the foetus during the first and second trimesters of pregnancy, but no controlled studies in pregnant women are available.

Voltaren Ophtha Eye Drops should not be used during the third trimester of pregnancy, due to possible risk of premature closure of the ductus arteriosus and possible inhibition of contractions (uterine inertia).

### Lactation

Following oral administration of 50 mg coated tablets (content of 10 bottles of 5 ml each of Voltaren Ophtha Eye Drops) only traces of the active substance were detected in breast milk and in quantities so small that no undesirable effects on the infant are to be expected.
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 experiencing blurred vision should refrain from driving a vehicle or operating machines.

## 4.8 Undesirable effects

**Immune system disorders:**
Rare: Eye allergy, eczema, systemic hypersensitivity reactions with dyspnoea, asthma, impulse to cough, acute rhinitis.

**Eye disorders:**
Common: Transient, mild to moderate eye irritation.
Rare: eye pruritus, eyelid pruritus, eyelid erythema, eyelid oedema, allergic conjunctivitis, conjunctival hyperaemia , corneal infiltrates, punctuate keratitis or corneal defects, postoperative mydriasis, eye pain, burning, ocular hyperaemia and blurred vision immediately after instillation of the eye drops.

**Gastrointestinal disorders:**
Uncommon: Nausea, vomiting

**Skin and subcutaneous tissue disorders:**
Rare: Urticaria, pruritus, redness, rash, delayed wound healing, photosensitivity.

In rare cases, prolonged use of topical diclofenac has been associated with corneal thinning and ulcer that could lead to a deterioration of vision in patients with risk factors for these conditions (e.g. use of corticosteroids) and/or concurrent infectious disease or rheumatoid arthritis.

## 4.9 Overdose

There is no experience of overdose with Voltaren Ophtha Eye Drops. However, inadvertent oral ingestion carries a minimal risk of adverse effects as a 5 mL bottle contains only 5 mg diclofenac sodium, corresponding to about 3% of the recommended maximum oral daily dose for an adult.

# 5 Pharmacological properties

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-inflammatory agents, non-steroids, ATC code: S01BC03.
Voltaren Ophtha Eye Drops contain diclofenac sodium, a non-steroidal anti-inflammatory agent with analgesic properties. It has marked prostaglandin synthesis inhibitory activity and this is thought to have an important bearing on its mechanism of action.

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.

There is no indication that diclofenac has any adverse effects on wound healing.
Voltaren Ophtha Eye Drops contains a cyclodextrin, hydroxypropyl gamma-cyclodextrin (HP-gamma-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. Elimination was rapid and almost complete after 6 hours.
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 for 28 days. Low concentrations of HP-gamma-CD were detected in the aqueous humor of two rabbits (1 after single instillation, 1 after q.i.d. instillation for 28 days).
Penetration of diclofenac into the anterior chamber has been confirmed in humans.

## 5.3 Preclinical safety data

Preclinical data of systemically applied diclofenac from acute and repeated dose toxicity studies, as well as from genotoxicity, mutagenicity, teratogenicity, carcinogenicity and reproductive performance studies revealed no specific hazard for humans at the intended therapeutic doses. Systemic diclofenac has been shown to cross the placental barrier in mice and rats, but had no influence on the fertility of parent animals in rats. In rats, maternally toxic doses were associated with dystocia, prolonged gestation, decreased foetal survival, and intrauterine growth retardation. The slight effects of diclofenac on fertility and delivery as well as constriction of the ductus arteriosus in utero are pharmacological consequences of this class of prostaglandin synthesis inhibitors. The potential for local ocular toxicity and associated systemic toxicity of Voltaren Ophtha Eye Drops and HP-gamma-CD were investigated in a series of ocular tolerance studies in rabbits. In these studies the rabbits received up to 8 instillations of 25 microliters of solution into the conjuctival sac of the right eye each day for up to 13 weeks. The left eye was untreated and

provided a control for local effects in the treated right eye. The animals received either Voltaren Ophtha Eye Drops with or without benzalkonium chloride or a formulation containing all of the excipients in Voltaren Ophtha Eye Drops but containing 0.1% diclofenac potassium (instead of 0.1% diclofenac sodium) as the active ingredient or a 2% solution of HP-gamma-CD in saline solution. In none of the studies was there any evidence of local adverse effects detectable by detailed ophthalmological and ocular histological examinations.

There was no evidence of systemic effects in the haematology, clinical chemistry, urinalysis parameters or in the histological examination of the liver, lungs and kidneys.

# 6 Pharmaceutical particulars

## 6.1 List of excipients

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

## 6.2 Incompatibilities

None known.

## 6.3 Special precautions for storage

Do not store above 25◦C. Close the bottle immediately after use. Do not use for more than one month after opening.
Voltaren Ophtha Eye Drops must be kept out of the reach and sight of children.

## 6.4 Nature and contents of container

The product is presented in a 5 mL white-coloured LDPE bottle fitted with a LDPE dropper and a HDPE closure.

## 6.5 Instructions for use and handling, and disposal

No special requirements.

## Manufacturer

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## License Holder

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