▼This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems.

AUSTRALIAN PRODUCT INFORMATION – VOLTAREN* OPHTHA (DICLOFENAC SODIUM) EYE DROPS SOLUTION

1 NAME OF THE MEDICINE

Diclofenac sodium.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

VOLTAREN* OPHTHA is sterile aqueous solution containing diclofenac sodium 1.0 mg/mL (0.1% w/v).

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Eye drops, solution.

Clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Reduction of post-operative inflammation in cataract surgery and other surgical interventions.

The single dose units can also be used to inhibit operative miosis during cataract surgery.

4.2 DOSE AND METHOD OF ADMINISTRATION

Adults

Pre-operatively: up to 5 drops during 3 hours before surgery.

Post-operatively: 1 drop 3 times on the day of surgery, followed by 1 drop 3 to 5 times daily.

Although systemic absorption of diclofenac sodium has been found to be minimal following ocular application, as a general precaution to reduce systemic absorption, pressure should be applied to the tear-duct immediately after application.

In clinical studies, effectiveness was demonstrated in patients treated throughout the first two weeks of the post-operative period. In some patients with persisting signs of inflammation, treatment continued for up to four weeks post-operatively.

To prevent the active substances from being washed out when additional ophthalmic medication is used, an interval of at least 5 minutes between each application should be adhered to.

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 as this may contaminate the solution.

4.3 CONTRAINDICATIONS

Patients with known hypersensitivity to diclofenac or other components of the medication.

Like other non-steroidal anti-inflammatory agents, VOLTAREN Ophtha eye drops is also contraindicated in patients in whom attacks of asthma, urticaria or acute rhinitis are precipitated by aspirin or by other medicines with prostaglandin-synthetase inhibiting activity. There is the potential for cross-sensitivity to aspirin, phenylacetic acid derivatives and other non-steroidal anti- inflammatory agents.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

As with other topically applied ophthalmic drugs, this drug may be absorbed systemically. However, in considering potential systemic toxicity, it should be noted that the effective daily dose of VOLTAREN Ophtha eye drops after ophthalmic administration corresponds to less than 1% of the daily dose recommended for VOLTAREN in rheumatic indications. In addition, application of 2 drops of 0.1% diclofenac sodium solution to each eye of healthy humans resulted in blood levels below the detection limit (10 ng/mL).

The anti-inflammatory activity of ophthalmic non-steroidal anti-inflammatory agents (NSAIDS) including diclofenac 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 VOLTAREN Ophtha eye drops.

Patients with evidence of corneal epithelial breakdown should immediately discontinue use of VOLTAREN Ophtha eye drops and should be monitored closely for corneal health.

Administer with caution in the presence of active gastrointestinal lesions or a history of recurrent gastrointestinal lesions.

There is a potential for increased bleeding time due to interference with thrombocyte aggregation with non-steroidal anti-inflammatory drugs. There have been reports (with other NSAIDs) of increased bleeding of ocular tissues in conjunction with ocular surgery. Caution should be used in surgical patients with known bleeding tendencies or who are receiving other medications that may prolong bleeding time.

There is a possibility that patients receiving other medications which may prolong bleeding time, or with known haemostatic defects may experience exacerbation with VOLTAREN Ophtha eye drops.

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 4.5 Interactions with other medicines and other forms of interactions).

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 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 contains benzalkonium chloride as a preservative; benzalkonium chloride may cause irritation and is known to discolour soft contact lenses. VOLTAREN Ophtha 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. The wearing of contact lenses is discouraged during treatment of an ocular inflammation.

Use in the elderly

No data available.

Paediatric use

VOLTAREN Ophtha is not indicated for use in children as safety and effectiveness have not been demonstrated in children.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF 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 including slow or delay corneal healing, therefore caution should be used.

A previous formulation of this product, which also contained 0.1% diclofenac sodium, has been used safely in clinical studies in combination with antibiotics and beta-blocking agents for ocular use.

Concomitant administration of voriconazole with diclofenac may increase plasma diclofenac levels.

Concomitant use of VOLTAREN Ophtha eye drops with medications that prolong bleeding time may increase the risk of haemorrhage.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on 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.

Use in Pregnancy (Category C)

NSAIDs inhibit prostaglandin synthesis and, when given during the latter part of pregnancy, may cause closure of the fetal ductus arteriosus, fetal renal impairment, inhibition of platelet aggregation, and delay labour and birth. 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. During the last few days before expected birth, agents with an inhibitory effect on prostaglandin synthesis should be avoided.

In addition, data from epidemiological studies suggest an increased risk of miscarriage after the use of prostaglandin synthesis inhibitor in early pregnancy.

Safety of diclofenac sodium in human pregnancy has not been established. Therefore VOLTAREN Ophtha should not be used during the first two trimesters of pregnancy or in women likely to become pregnant, unless the expected benefits to the mother outweigh the risks to the foetus. VOLTAREN Ophtha should not be used during the third trimester of pregnancy.

Use in Lactation

No measurable amounts of active substance are to be expected in the breast milk of nursing mothers. However, since no experience has been acquired with VOLTAREN Ophtha during lactation, it is not recommended for use in this circumstance.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Patients experiencing blurred vision or other visual disturbances should refrain from driving a vehicle or operating machines until vision clears (see Section 4.8 Adverse Effects (Undesirable Effects)).

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

In clinical studies with VOLTAREN Ophtha eye drops, the following adverse events have been reported:

Incidence greater than 10 %	- a mild to moderate eye irritation (approximately 13%).
Incidence 1 to 10 %	- keratitis/punctate keratitis/ulceration (approximately 2%). - elevated intraocular pressure, particularly in patients post-surgery, but not at a frequency consistently higher than placebo-treated patients.
Incidence less than 1%	- blurred vision immediately after instillation of the eye drops; hypersensitivity reactions with pruritis and ocular hyperaemia; photosensitivity. - permanent post-operative mydriasis has been reported (a causality has not been established). - systemic reactions have been reported at a rate (1%) not significantly higher than in placebo-treated patients.

Corneal disorders have also been reported 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, punctate keratitis, corneal epithelial defect or corneal oedema which may become sight-threatening. Most patients were treated for a prolonged period of time.

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

Allergic conditions such as conjunctival hyperaemia, allergic conjunctivitis, eyelid erythema, eye allergy, eyelid oedema, eyelid pruritis, urticaria, rash, eczema, erythema, pruritis, hypersensitivity, cough and rhinitis have been reported. Another less frequently observed reaction is eye pain.

Post Marketing Experience

The following adverse reactions have been reported during Alcon clinical studies with VOLTAREN Ophtha 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.

Eye disorders

Common (≥ 1% to < 10%): punctate keratitis, eye pain, eye irritation, eye pruritus, conjunctival hyperaemia.

Uncommon (≥ 0.1% to < 1%): 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.

Immune system disorders

Uncommon (≥ 0.1% to < 1%): hypersensitivity.

General disorders and administration site conditions

Uncommon (≥ 0.1% to < 1%): impaired healing.

The following adverse reactions have been identified from post-marketing surveillance following administration of VOLTAREN Ophtha. Frequency cannot be estimated from the available data. Within each System Organ Class adverse reactions are presented in order of decreasing seriousness.

Eye disorders

Not Known: corneal perforation, ulcerative keratitis, corneal epithelium defect, corneal opacity, corneal thinning, allergic conjunctivitis, eye allergy, eyelid erythema, eyelid oedema, eyelid pruritus, vision blurred.

Infections and infestations

Not Known: rhinitis.

Respiratory, thoracic and mediastinal disorders

Not Known: asthma exacerbations, dyspnoea, cough.

Skin and subcutaneous tissue disorders

Not Known: urticaria, rash, eczema, erythema, pruritus.

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

There is no experience of overdose with VOLTAREN Ophtha eye drops. However, accidental oral ingestion carries a minimal risk of adverse effects, since the eye drop solution in a 5mL bottle contains only 5mg diclofenac sodium corresponding to about 3% of the maximum recommended daily adult dose of VOLTAREN Ophtha for oral administration.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

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

VOLTAREN Ophtha eye drops contain diclofenac sodium, a non-steroidal compound with 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 VOLTAREN Ophtha has been found to inhibit miosis during cataract surgery and to reduce inflammation following surgical interventions.

The effective daily dose after ocular application of VOLTAREN Ophtha eye drops (approx. 0.25-0.5 mg diclofenac sodium) corresponds less than 1% of the daily dose recommended for

VOLTAREN in rheumatic indications.

The benzalkonium chloride containing formulation of VOLTAREN Ophtha eye drops contains a cyclodextrin, hydroxypropylbetadex. Cyclodextrins (CDs) increase the aqueous solubility of some lipophilic water-soluble 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.

Penetration of diclofenac into the anterior chamber has been confirmed in humans. No measurable plasma levels of diclofenac (limit of detection 10 ng/mL) could be found in 22 human subjects after ocular application of a multidose formulation of 0.1% diclofenac sodium eye drops preserved with sorbic acid.

The pharmacokinetics of the reformulated multidose product were not studied in humans and were not compared with the pharmacokinetics of the original multidose formulation.

5.3 PRECLINICAL SAFETY DATA

Carcinogenicity and Mutagenicity

Dietary administration of diclofenac to mice and rats at doses up to 0.5 mg/kg/day revealed no carcinogenic activity. However, the plasma concentration of diclofenac at this dose level was 20 to 100 times lower than that in humans after oral administration. Administration of higher doses to rats and mice resulted in increased mortality due to gastrointestinal ulceration. Diclofenac showed no mutagenic effects in the studies conducted.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Benzalkonium chloride (50 µg/mL as preservative), disodium edetate, hydroxypropylbetadex, hydrochloric acid, propylene glycol, trometamol, tyloxapol and water for injections.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Protect from light. Do not freeze. Discard 4 weeks after opening

6.5 NATURE AND CONTENTS OF CONTAINER

VOLTAREN Ophtha is available in LDPE bottles containing 3 mL and 5 mL solution.

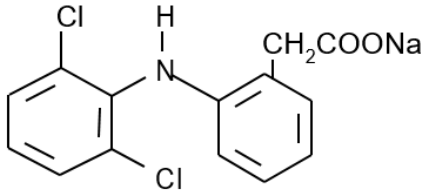
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Diclofenac sodium, is a yellowish-white, odourless, crystalline powder sparingly soluble in water.

Chemical structure



Chemical name: sodium [2-(2,6-dichloroanilino)phenyl] acetate, a phenylacetic acid derivative

Molecular formula: $C_{14}H_{10}Cl_2NNaO_2$

Molecular weight: 318.1

CAS number

15307-79-6

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription medicine

8 SPONSOR

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9 DATE OF FIRST APPROVAL

20 July 2005

10 DATE OF REVISION

03 January 2023

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.6	Revised wording to emphasise that Voltaren Ophtha should not be used in the first and second trimester.