Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

VEXOL 10mg/ml eye drops, suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of suspension contains 10mg of Rimexolone

Excipients: 1 ml of suspension contains 0.1mg of benzalkonium chloride.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, suspension
Vexol is a white to off-white suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

VEXOL is indicated for the treatment of postoperative inflammation following ocular surgery, for the treatment of anterior uveitis, and for the treatment of corticosteroid responsive inflammation of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe. The inflammation should be of a non-infectious nature. In more serious cases, and if the posterior part of the globe is affected, subconjunctival injection or systemic treatment is recommended (see section 4.4).

4.2 Posology and method of administration

Route of administration: Ocular use.

Postoperative Inflammation

Apply one drop of VEXOL into the conjunctival sac of the affected eye four times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the postoperative period. There are no clinical data on the use of VEXOL immediately after surgery.

Steroid Responsive Inflammation

Apply one drop of VEXOL into the conjunctival sac of the affected eye four times or more daily. The duration of treatment should be determined by the prescribing physician according to the severity of the disease, but should not exceed four weeks.

Uveitis

Apply one drop of VEXOL into the conjunctival sac of the affected eye every hour during the daytime for the first week, one drop every two hours during the daytime of the second week, four times per day during the third week; then twice per day during the first 4 days of week four and then once per day during the last 3
days of week four. Alternative dosing may be appropriate in some circumstances.

Use in older people

Clinical studies have indicated that dosage modifications are not required for use in older people.

Use in children

Safety and effectiveness in children have not been established.

Use in hepatic and renal impairment

No clinical experience in patients with impaired renal or hepatic function is available.

Instructions for Use

Shake well before use. Do not touch dropper tip to any surface, as this may contaminate the suspension. Keep the bottle tightly closed when not in use.

After cap is removed, if tamper evident snap collar is loose, remove before using product.

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients listed in section 6.1.

VEXOL is contraindicated in epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, and most other viral diseases of cornea and conjunctiva; mycobacterial infection of the eye; fungal diseases of the eye; acute purulent untreated infections which, like other diseases caused by microorganisms may be masked or enhanced by the presence of the steroid; red eye, where the diagnosis is unconfirmed; and amoebic infections.

4.4 Special warnings and precautions for use

For ocular use only. Not for injection or oral ingestion.

In more serious cases, and if the posterior part of the globe is affected, subconjunctival injection or treatment is recommended.

Prolonged use may result in ocular hypertension/glaucoma, damage to the optic nerve, reduced visual acuity and visual field defects, and posterior subcapsular cataract formation. It is advisable that the intraocular pressure be checked frequently. This is especially important in paediatric patients, as the risk of corticosteroid-induced ocular hypertension may be greater in children and may occur earlier than in adults. VEXOL is not approved for use in paediatric patients.

The risk of corticosteroid-induced raised intraocular pressure and/or cataract formation is increased in predisposed patients (e.g. diabetics, high myopes, family history of glaucoma and young children).
Prolonged use may also result in secondary bacterial, viral or fungal ocular infections due to suppression of host response. Acute purulent infections of the eye may be masked or exacerbated by the presence of corticosteroid medication.

In those diseases causing thinning of the cornea or sclera, perforation has been known to occur with topical steroids.

General: Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been or is in use.

Topical ophthalmic corticosteroids may slow corneal wound healing. Topical NSAIDs are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems. (See section 4.5).

The wearing of contact lenses (hard or soft) is discouraged during treatment of an ocular inflammation. If patients are allowed to wear contact lenses, VEXOL should not be instilled while wearing contact lenses. Lenses should not be

inserted for 15 minutes after instillation of VEXOL. Additionally, the preservative benzalkonium chloride may cause eye irritation and is known to discolour soft lenses.

4.5 Interaction with other medicinal products and other forms of interaction

Specific drug interaction studies have not been conducted with VEXOL. No drug interactions were identified during the clinical development program.

Concomitant use of topical steroids and topical NSAIDs may increase the potential for corneal healing problems.

If more than one topical ophthalmic medicinal product is being used, the medicines must be administered at least 5 minutes apart. Eye ointments should be administered last.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amounts of data from the use of VEXOL in pregnant women.

Studies with corticosteroids in animals have shown reproductive toxicity (see section 5.3). The potential risk for humans is unknown.

VEXOL should not be used during pregnancy unless clearly necessary.

Infants born to mothers who have received substantial doses of corticosteroids during pregnancy should be observed carefully for signs of hypoadrenalism.

Breast-feeding

It is unknown whether rimexolone/metabolites are excreted in human milk. A risk to the newborn infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from VEXOL therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman..
Fertility

Studies have not been performed to evaluate the effect of topical ocular administration of rimexolone on human fertility.

4.7 Effects on ability to drive and use machines

VEXOL has no or negligible influence on the 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 or visual disturbances occur after instillation, the patient must wait until the vision clears before driving or using machinery.

4.8 Undesirable effects

In clinical studies involving 1346 patients using VEXOL, the most frequently reported adverse drug reactions were: vision blurred, eye discharge and ocular discomfort, occurring in approximately 1% to 2% of patients.

The following adverse reactions were reported during clinical trials and post-marketing experience with VEXOL: Adverse reactions are classified according to the following 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), very rare (<1/10,000), or not known (cannot be estimated from the available data). Within each frequency-grouping, adverse reactions are presented in order of decreasing seriousness.

System Organ Classification	MedDRA Preferred Term (v.15.0)

Infections and infestations	*Uncommon*: pharyngitis *Rare:* rhinitis
Immune system disorders	*Rare*: hypersensitivity
Nervous system disorders	*Uncommon*: headache
Eye disorders	*Common*: vision blurred, ocular discomfort, eye discharge *Uncommon*: keratitis, ocular oedema, corneal oedema, eye pain, eye irritation, dry eye, lacrimation increased, corneal stainingeye pruritus, intraocular pressure increased, ocular hyperaemia *Rare:* corneal erosion, ulcerative keratitis, macular oedema, anterior chamber fibrin, corneal infiltrates, photophobia, eyelid oedema, eyelid margin crusting *Not known:* visual acuity reduced
Vascular disorders	*Rare*: hypotension
Gastrointestinal disorders	*Uncommon:* dysgeusia
General disorders and administration site conditions	*Not known*: chest pain

Description of selected adverse reactions

- Prolonged use of topical ophthalmic corticosteroids may result in increased intraocular pressure with damage to the optic nerve, reduced visual acuity and visual field defects, and posterior subcapsular cataract formation (See Section 4.4).
- The development of secondary infections has occurred after the use of corticosteroids (See Section 4.4).
- In those diseases causing thinning of the cornea or sclera there is a higher risk for perforation (See Section 4.4).

Reporting of suspected adverse reactions
Reporting of 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

A topical overdose is not likely to be associated with toxicity. A topical overdosage of VEXOL may be flushed from the eye(s) with luke warm tap water.

Accidental oral ingestion is also unlikely to be associated with toxicity. Treatment of a suspected ingestion is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: SO1BA13, Ophthalmological anti-inflammatory corticosteroid.

Corticosteroids suppress the inflammatory response to a variety of inciting agents of a mechanical, chemical, or immunological nature. They prevent or suppress redness, swelling, tenderness, exudation, cellular infiltration, capillary dilation, fibroblastic proliferation, deposition of collagen and late cicatrization. Placebo controlled clinical studies demonstrated that VEXOL is efficacious for the treatment of anterior chamber inflammation following cataract surgery.

In two controlled clinical trials, VEXOL demonstrated clinical and statistical equivalence to 1% prednisolone acetate in controlling uveitic inflammation. Supportive studies have confirmed the anti-inflammatory activity of VEXOL in steroid responsive ocular inflammation.

Corticosteroids are capable of producing a rise in intraocular pressure in susceptible individuals. In a controlled 6 week study of steroid responsive subjects the time to raise intraocular pressure was similar for VEXOL and 0.1% fluorometholone given four times daily.

5.2 Pharmacokinetic properties

As with other topically administered drugs, VEXOL is absorbed systemically. Studies in normal volunteers dosed bilaterally once every hour during waking hours for one week have demonstrated maximal serum concentrations ranging from less than 80 pg/mL to approximately 460 pg/mL. The mean maximal serum concentrations were approximately 150 pg/mL (n = 15). Serum concentrations were at or near steady state on day one of the dosing regimen. After decreasing the dosing frequency to once every two hours while awake during the second week of administration, mean maximal serum concentrations were approximately 100 pg/mL. The serum half-life of rimexolone could not be reliably estimated due to the large number of samples below the quantitation limit of the assay (80 pg/mL). However, based on the time required to reach steady-state, the half-life appears to be short (1-2 hours).

Based upon *in vivo* and *in vitro* preclinical metabolism studies and on *in vitro* results with human liver preparations, Rimexolone undergoes extensive metabolism with primary (> 80%) excretion via the faeces. Metabolites have been shown to be less active than parent drug, or inactive in human glucocorticoid binding assays.

5.3 Preclinical safety data

Carcinogenesis, mutagenesis, impairment of fertility: Rimexolone has been shown to be not mutagenic in a battery of *in vitro* and *in vivo* mutagenicity assays. Fertility and reproductive capability was not impaired in a study in rats with plasma levels (42 nanograms/mL) approximately 200 times those obtained in clinical studies after topical administration (< 0.2 nanogram/mL). Long-term studies have not been conducted in animals to evaluate the carcinogenic potential of rimexolone.

Rimexolone has been shown to be teratogenic and embryotoxic in rabbits following subcutaneous administration, but was not teratogenic or embryotoxic in rats. Corticosteroids are recognized to cause foetal resorptions and malformations in animals, though the association in humans has not been firmly established.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
Mannitol (E421)
Carbomer
Polysorbate 80 (E433)
Sodium chloride
Disodium edetate
Sodium hydroxide and/or hydrochloric acid (for pH adjustment)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

1 year for the 3 mL bottle.
2 years for the 5 mL and 10 mL bottles.
After first opening: 4 weeks

6.4 Special precautions for storage

Do not store above 30°C. Do not freeze.

6.5 Nature and contents of container

Low density polyethylene bottles (droptainer) containing 3 mL, 5 mL, or 10 mL and with polypropylene screw caps.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Alcon Laboratories (UK) Ltd
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Surrey, GU16 7SR
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA0290/073/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 07 March 1997

Date of last renewal: 20 July 2010

10 DATE OF REVISION OF THE TEXT

May 2016