

VEXOL[®] (rimexolone) 1% EYE DROPS SUSPENSION

Rimexolone 10 mg/mL

Presentation

VEXOL[®] (rimexolone) 1% Eye Drops is a sterile, topical, anti-inflammatory corticosteroid for ophthalmic use. VEXOL is a white to off-white suspension.

VEXOL is an isotonic suspension with an osmolality of approximately 300 mOsmol/kg. VEXOL has a physiologic pH of approximately 7.2.

Uses

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[®] Eye Drops is efficacious for the treatment of anterior chamber inflammation following cataract surgery.

Pharmacokinetics

As with other topically administered drugs, VEXOL[®] Eye Drops 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.

Indications

VEXOL[®] Eye Drops 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.

Dosage and administration

Postoperative Inflammation

Apply one drop of VEXOL[®] Eye Drops suspension 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[®] Eye Drops suspension 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[®] Eye Drops suspension into the conjunctival sac of the affected eye every hour while awake for the first week, one drop every two hours while awake 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.

Contraindications

Hypersensitivity to the active substance or any of the excipients.

VEXOL[®] Eye Drops 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.

Warnings and precautions

In more serious cases, and if the posterior part of the globe is affected, subconjunctival injection or treatment is recommended. But VEXOL[®] Eye Drops is not for injection. Prolonged use may result in ocular hypertension/glaucoma, damage to the optic nerve, defects in visual acuity and visual fields, and posterior subcapsular cataract formation. Prolonged use may also result in secondary 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. It is advisable that the intraocular pressure be checked frequently.

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.

The wearing of contact lenses (hard or soft) is discouraged during treatment of an ocular inflammation. VEXOL[®] Eye Drops should not be instilled while wearing contact lenses; lenses should not be inserted for 15 minutes after instillation of VEXOL.

Actions the health care professional should take

Systemic absorption can be minimised if patients are instructed to gently occlude the nasolacrimal ducts for two minutes immediately after instillation of the eye drop.

Use in Pregnancy - Category

There are no adequate data from controlled clinical studies for the use of rimexolone in pregnant women.

Preclinical studies have shown reproductive toxicity in rabbits only. The potential risk for humans is unknown.

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

VEXOL[®] Eye Drops should not be used during pregnancy unless it is clearly necessary.

Use in Lactation

It is not known whether topical ophthalmic administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human breast milk. Nevertheless, caution should be exercised when topical corticosteroids are administered to a nursing woman; a decision should be made whether to discontinue nursing or discontinue therapy, taking into consideration the importance of the drug to the mother.

Paediatric use

Safety and effectiveness in children have not been established.

Use in the Elderly

Clinical studies have indicated that dosage modifications are not required for use in the elderly.

Hepatic/Renal Impairment

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

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.

Adverse effects

In clinical studies with VEXOL[®] Eye Drops, the most frequently reported adverse events and local symptoms were: blurred vision (2.6%) and ocular discharge (2.2%).

The following undesirable effects were reported during clinical trials with VEXOL:

Infections and Infestations

Uncommon (> 0.1% to ≤ 1%): rhinitis, pharyngitis.

Nervous System Disorders

Uncommon (> 0.1% to ≤ 1%): headache (including browache), dysgeusia (taste perversion).

Eye Disorders:

Common (> 1% to ≤ 10%): vision blurred, eye discharge, ocular discomfort, eye pain, foreign body sensation in eye.

Uncommon (> 0.1% to ≤ 1%): ocular hyperaemia, eye pruritus, abnormal sensation in eye (sticky sensation), anterior chamber fibrin, dry eye, conjunctival oedema, keratitis, lacrimation increased, photophobia, eye oedema, eye irritation, corneal ulcer, eyelid margin crusting, corneal oedema, corneal infiltrates, corneal erosion.

Vascular Disorders

Uncommon (> 0.1% to ≤ 1%): hypotension.

Investigations:

Common (> 1% to ≤ 10%): intraocular pressure increased.

Uncommon (> 0.1% to ≤ 1%): corneal staining.

In post-marketing experience, the most frequently reported events are eye irritation, lid margin crusting, ocular hyperaemia and intraocular pressure increase. These events are similar to those identified during clinical trials.

Use of topical corticosteroids may cause increased intraocular pressure.

Interactions

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

If concomitant eye preparations are to be used, the patient should be advised to wait about 15 minutes between the two applications.

Effects on ability to drive and use machines

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

Overdosage

A topical overdose is not likely to be associated with toxicity. A topical overdosage of VEXOL[®] Eye Drops may be flushed from the eye(s) with lukewarm tap water.

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

Pharmaceutical precautions

Store below 30 °C. Do not freeze.

Discard four weeks after opening.

Medicine classification

Prescription Medicine.

Package quantities

VEXOL[®] Eye Drops is supplied in 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. Tamper evidence is provided with a shrink band around the closure and neck area of the package.

Consumer Medicine Information is supplied with this product.

Further information

Clinical Studies

In two controlled clinical trials, VEXOL[®] Eye Drops 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.

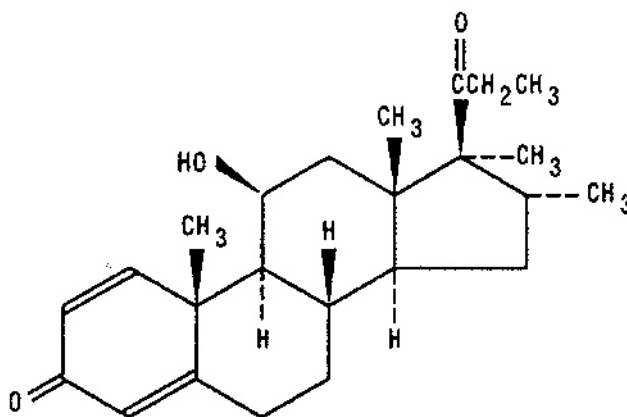
Contact lenses

VEXOL[®] 1% Eye Drops should not be administered while wearing contact lenses. If patients continue to wear soft (hydrophilic) contact lenses while under treatment with VEXOL they should remove their lens(es) prior to instilling VEXOL in the affected eye(s) and should not insert their lens(es) until 15 minutes after instillation of the eye drops.

List of excipients

Active: rimexolone (10 mg/mL). **Inactives:** benzalkonium chloride, mannitol, carbomer, polysorbate 80, sodium chloride, disodium edetate, sodium hydroxide and/or hydrochloric acid and pureed water.

Rimexolone is a yellow crystalline or powder substance. Each mL of VEXOL[®] Eye Drops contains 10 mg of rimexolone. The chemical structure is:



Molecular weight: 370.53

Empirical formula: C₂₄H₃₄O₃

Chemical name: 11 β -Hydroxy-16 α ,17 α -dimethyl-17-propionylandrosta-1,4-dien-3-one

CAS Number: 49697-38-3

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