LOTEMAX® (loteprednol etabonate ophthalmic gel) 0.5%, for topical ophthalmic use

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

LOTEMAX® is a corticosteroid indicated for the treatment of postoperative inflammation and pain following ocular surgery. (1)

2 DOSAGE AND ADMINISTRATION

• Invert closed bottle and shake once to fill tip before instilling drops. (2)

• Apply one to two drops of LOTEMAX into the conjunctival sac of the affected eye four times daily beginning the day after surgery and continuing throughout the first 2 weeks of the postoperative period. (2)

3 DOSAGE FORMS AND STRENGTHS

LOTEMAX is a sterile preserved ophthalmic gel containing 5 mg of loteprednol etabonate per gram of gel. (3)

4 CONTRAINDICATIONS

LOTEMAX is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, in mycobacterial infection of the eye and fungal diseases of ocular structures. (4)

5 WARNINGS AND PRECAUTIONS

5.1 Intraocular Pressure (IOP) Increase

Intraocular pressure should be monitored. (5.1)

5.2 Cataracts

Use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. If this product is used for 10 days or longer, IOP should be monitored. (5.1)

5.3 Delayed Healing

The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining. (5.3)

5.4 Bacterial Infections

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. If this product is used for 10 days or longer, IOP should be monitored. (5.1)

5.5 Viral Infections

The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining. (5.3)

5.6 Fungal Infections

Fungal infections – 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 used or is in use. (5.6)

5.7 Contact Lens Wear

Patients should not wear contact lenses during their course of therapy with LOTEMAX. (5.7)

6 ADVERSE REACTIONS

The most common adverse drug reactions (2-5%) were anterior chamber inflammation, eye pain, and foreign body sensation. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Bausch + Lomb, a division of Valeant Pharmaceuticals North America LLC, at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

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5.4 Bacterial Infections

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions of the eye, steroids may mask infection or enhance existing infection.

5.5 Viral Infections

Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex). (5.5)

5.6 Fungal Infections

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 used or is in use. Fungal cultures should be taken when appropriate.

5.7 Contact Lens Wear

Patients should not wear contact lenses during their course of therapy with LOTEMAX.

6 ADVERSE REACTIONS

Adverse reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with infrequent optic nerve damage, visual field defects, posterior subcapsular cataract formation, delayed wound healing and secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera.

The most common adverse drug reactions reported in the clinical trials (2-5%) were anterior chamber inflammation, eye pain, and foreign body sensation.

7 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies with loteprednol etabonate in pregnant women.

Loteprednol etabonate produced teratogenicity at clinically relevant doses in the rabbit and rat when administered orally during pregnancy. Loteprednol etabonate produced malformations...
when administered orally to pregnant rabbits at doses ≥1.2 times the recommended human oral dose (RHOD) and to pregnant rats at doses ≥30 times the RHOD. In pregnant rats receiving oral doses of loteprednol etabonate during the period equivalent to the last trimester of pregnancy through lactation in humans, survival of offspring was reduced at doses ≥3 times the RHOD. Maternal toxicity was observed in rats at doses ≥304 times the RHOD, and a maternal no observed adverse effect level (NOAEL) was established at 30 times the RHOD.

The background risk of major birth defects and miscarriage for the indicated population is unknown. However, the background risk in the U.S. general population of major birth defects is 2 to 4%, and of miscarriage is 15 to 20%, of clinically recognized pregnancies.

Data

Animal Data

Embryofetal studies were conducted in pregnant rabbits administered loteprednol etabonate by oral gavage on gestation days 6 to 18, to target the period of organogenesis. Loteprednol etabonate produced fetal malformations at doses ≥0.1 mg/kg (1.2 times the recommended human oral dose (RHOD) based on body surface area, assuming 100% absorption). Spina bifida (including meningocoele) was observed at doses ≥0.1 mg/kg, and exencephaly and craniofacial malformations were observed at doses ≥0.4 mg/kg (4.9 times the RHOD); At 3 mg/kg (36 times the RHOD), loteprednol etabonate was associated with increased incidences of abnormal left common carotid artery, limb flexures, umbilical hernia, scoliosis, and delayed ossification. Abortion and embryofetal lethality (resorption) occurred at doses ≥6 mg/kg (73 times the RHOD). A NOAEL for developmental toxicity was not established in this study. The NOAEL for maternal toxicity in rabbits was 3 mg/kg/day.

Embryofetal studies were conducted in pregnant rats administered loteprednol etabonate by oral gavage on gestation days 6 to 15, to target the period of organogenesis. Loteprednol etabonate produced fetal malformations, including absent innominate artery at doses ≥5 mg/kg (30 times the RHOD); and cleft palate, agnathia, cardiovascular defects, umbilical hernia, decreased fetal body weight and decreased skeletal ossification at doses ≥50 mg/kg (304 times the RHOD). Embryofetal lethality (resorption) was observed at 100 mg/kg (608 times the RHOD). The NOAEL for developmental toxicity in rats was 0.5 mg/kg (3 times the clinical dose), reduced survival was observed in live-born offspring. Doses ≥5 mg/kg (30 times the RHOD) caused umbilical hernia/incomplete gastrointestinal tract. Doses ≥50 mg/kg (304 times the RHOD) produced maternal toxicity (reduced body weight gain, death), decreased number of live-born offspring, decreased birth weight, and delays in postnatal development. A developmental NOAEL was not established in this study. The NOAEL for maternal toxicity was 5 mg/kg.

8.2 Lactation

There are no data on the presence of loteprednol etabonate in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother’s clinical need for LOTEMAX and any potential adverse effects on the breastfed infant from LOTEMAX.

8.4 Pediatric Use

The safety and effectiveness of LOTEMAX have been established in the pediatric population. Use of LOTEMAX in this population is supported by evidence from adequate and well-controlled trials of LOTEMAX in adults with additional data from a safety and efficacy trial in pediatric patients from birth to 11 years of age [see Clinical Studies (14)].

8.5 Geriatric Use

No overall differences in safety and effectiveness have been observed between elderly and younger patients.

11 DESCRIPTION

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