

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
202872Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use LOTEMAX® (loteprednol etabonate ophthalmic gel) 0.5% safely and effectively. See full prescribing information for LOTEMAX®.

LOTEMAX® (loteprednol etabonate ophthalmic gel) 0.5%

Initial U.S. Approval: 1998

-----**INDICATIONS AND USAGE**-----

LOTEMAX is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery. (1)

-----**DOSAGE AND ADMINISTRATION**-----

Invert closed bottle and shake once to fill tip before instilling drops.

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 post-operative period. (2)

-----**DOSAGE FORMS AND STRENGTHS**-----

LOTEMAX contains 5 mg/g of loteprednol etabonate, as a sterile preserved ophthalmic gel. (3)

-----**CONTRAINDICATIONS**-----

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

-----**WARNINGS AND PRECAUTIONS**-----

- Intraocular pressure (IOP) increase - 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)
- Cataracts- Use of corticosteroids may result in posterior subcapsular cataract formation. (5.2)

- 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)
- Bacterial infections--Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infection. In acute purulent conditions, steroids may mask infection or enhance existing infection. (5.4)
- 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)
- 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)

-----**ADVERSE REACTIONS**-----

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

To report SUSPECTED ADVERSE REACTIONS, contact Bausch & Lomb at 1-800-323-0000 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

See [17](#) for PATIENT COUNSELING INFORMATION

Revised: 9/2012

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*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

LOTEMAX is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

2 DOSAGE AND ADMINISTRATION

Invert closed bottle and shake once to fill tip before instilling drops.

Apply one to two drops of LOTE MAX 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 post-operative period.

3 DOSAGE FORMS AND STRENGTHS

LOTEMAX (loteprednol etabonate ophthalmic gel) 0.5% contains 5 mg/g of loteprednol etabonate, as a sterile preserved ophthalmic gel.

4 CONTRAINDICATIONS

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

5 WARNINGS AND PRECAUTIONS

5.1 Intraocular Pressure (IOP) Increase

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. If this product is used for 10 days or longer, intraocular pressure should be monitored.

5.2 Cataracts

Use of corticosteroids may result in posterior subcapsular cataract formation.

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.

5.4 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).

5.6 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 LOTE MAX.

6 ADVERSE REACTIONS

Adverse reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with infrequent optic nerve damage, visual acuity and 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 were anterior chamber inflammation (5%), eye pain (2%), and foreign body sensation (2%).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic effects: Pregnancy Category C

Loteprednol etabonate has been shown to be embryotoxic (delayed ossification) and teratogenic (increased incidence of meningocele, abnormal left common carotid artery, and limb flexures) when administered orally to rabbits during organogenesis at a dose of 3 mg/kg/day (35 times the maximum daily clinical dose), a dose which caused no maternal toxicity. The no-observed-effect-level (NOEL) for these effects was 0.5 mg/kg/day (6 times the maximum daily clinical dose). Oral treatment of rats during organogenesis resulted in teratogenicity (absent innominate artery at ≥ 5 mg/kg/day doses, and cleft palate and umbilical hernia at ≥ 50 mg/kg/day) and embryotoxicity (increased post-implantation losses at 100 mg/kg/day and decreased fetal body weight and skeletal ossification with ≥ 50 mg/kg/day). Treatment of rats with 0.5 mg/kg/day (6 times the

maximum clinical dose) during organogenesis did not result in any reproductive toxicity. Loteprednol etabonate was maternally toxic (significantly reduced body weight gain during treatment) when administered to pregnant rats during organogenesis at doses of ≥ 5 mg/kg/day.

Oral exposure of female rats to 50 mg/kg/day of loteprednol etabonate from the start of the fetal period through the end of lactation, a maternally toxic treatment regimen (significantly decreased body weight gain), gave rise to decreased growth and survival, and retarded development in the offspring during lactation; the NOEL for these effects was 5 mg/kg/day. Loteprednol etabonate had no effect on the duration of gestation or parturition when administered orally to pregnant rats at doses up to 50 mg/kg/day during the fetal period.

There are no adequate and well controlled studies in pregnant women. LOTEMAX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers

It is not known whether topical ophthalmic administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Systemic steroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Caution should be exercised when LOTEMAX is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

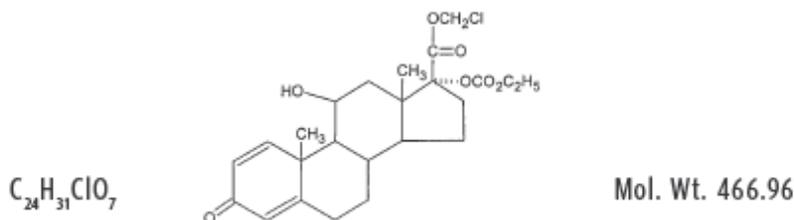
8.5 Geriatric Use

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

11 DESCRIPTION

LOTEMAX (loteprednol etabonate ophthalmic gel) 0.5% contains a sterile, topical corticosteroid for ophthalmic use. Loteprednol etabonate is a white to off-white powder.

Loteprednol etabonate is represented by the following structural formula:



Chemical Name:

chloromethyl 17 α -[(ethoxycarbonyl)oxy]-11 β -hydroxy-3-oxoandrosta-1,4-diene-17 β -carboxylate

Each gram contains:

ACTIVE: Loteprednol Etabonate 5 mg (0.5%);

INACTIVES: Boric acid, edetate disodium dihydrate, glycerin, polycarbophil, propylene glycol, sodium chloride, tyloxapol, water for injection, and sodium hydroxide to adjust to a pH of between 6 and 7.

PRESERVATIVE: benzalkonium chloride 0.003%.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Corticosteroids inhibit the inflammatory response to a variety of inciting agents and probably delay or slow healing. They inhibit the edema, fibrin deposition, capillary dilation, leukocyte migration, capillary proliferation, fibroblast proliferation, deposition of collagen, and scar formation associated with inflammation. While glucocorticoids are known to bind to and activate the glucocorticoid receptor, the molecular mechanisms involved in glucocorticoid/gluco-corticoid receptor-dependent modulation of inflammation are not clearly established. However, corticosteroids are thought to inhibit prostaglandin production through several independent mechanisms.

12.3 Pharmacokinetics

Loteprednol is lipid soluble and can penetrate into cells. Loteprednol etabonate is synthesized through structural modifications of prednisolone-related compounds so that it will undergo a predictable transformation to an inactive metabolite. Based upon *in vivo* and *in vitro* preclinical metabolism studies, loteprednol etabonate undergoes extensive metabolism to the inactive carboxylic acid metabolites, PJ-91 and PJ-90. The systemic exposure to loteprednol etabonate following ocular administration of LOTEMAX has not been studied in humans.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment Of Fertility

Long-term animal studies have not been conducted to evaluate the carcinogenic potential of loteprednol etabonate. Loteprednol etabonate was not genotoxic *in vitro* in the Ames test, the mouse lymphoma tk assay, or in a chromosome aberration test in human lymphocytes, or *in vivo* in the

single dose mouse micronucleus assay. Treatment of male and female rats with up to 50 mg/kg/day and 25 mg/kg/day of loteprednol etabonate, respectively, (600 and 300 times the maximum clinical dose, respectively) prior to and during mating did not impair fertility in either gender.

14 CLINICAL STUDIES

In two randomized, multicenter, double-masked, parallel-group, vehicle-controlled studies in 813 subjects with, post-operative inflammation, LOTEMAX was more effective compared to its vehicle in resolving anterior chamber inflammation and pain following cataract surgery. Primary endpoints were complete resolution of anterior chamber cells (cell count of 0) and no pain at post-operative day 8.

In these studies, LOTEMAX had a statistically significant higher incidence of subjects with complete clearing of anterior chamber cells (31% vs. 14-16%) and were pain free at post-operative day 8 (73-76% vs. 42-46%).

16 HOW SUPPLIED/STORAGE AND HANDLING

LOTEMAX (loteprednol etabonate ophthalmic gel) 0.5% is a sterile ophthalmic gel supplied in a white low density polyethylene plastic bottle with a white controlled drop tip and a pink polypropylene cap in the following size:

5 g in a 10 mL bottle (NDC 24208-503-07)

Use only if imprinted neckband is intact.

Storage: Store upright at 15°-25° C (59°-77° F).

17 PATIENT COUNSELING INFORMATION

17.1 Administration

Invert closed bottle and shake once to fill tip before instilling drops.

17.2 Risk of Contamination

Patients should be advised not to allow the dropper tip to touch any surface, as this may contaminate the gel.

17.3 Contact Lens Wear

Patients should be advised not to wear contact lenses when using LOTEMAX.

17.4 Risk of Secondary Infection

If pain develops, redness, itching or inflammation becomes aggravated, the patient should be advised to consult a physician.

Bausch & Lomb Incorporated
Tampa, Florida 33637 USA

US Patent No. 5,800,807

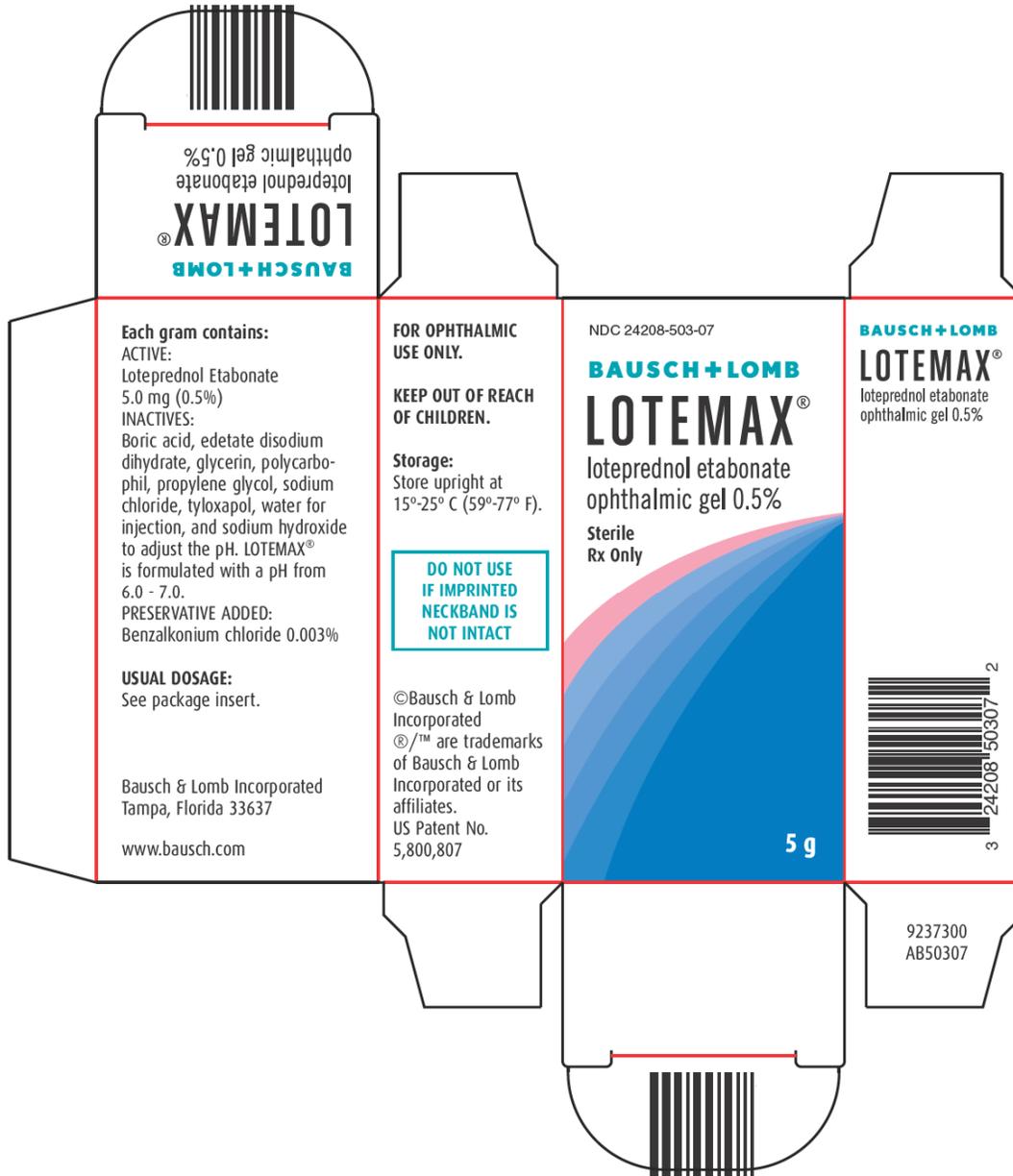
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Trade Container Label – 5g/10 mL bottle:

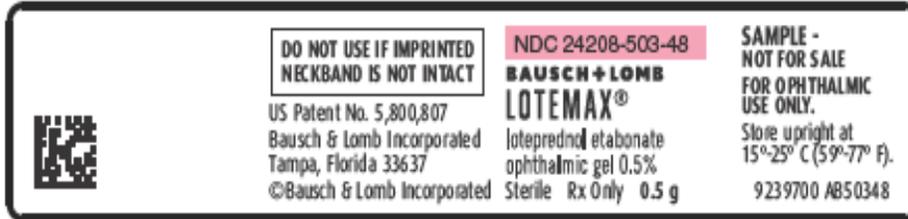
DO NOT USE IF IMPRINTED NECKBAND IS NOT INTACT	NDC 24208-503-07	Each gram contains: ACTIVE: Loteprednol Etabonate 5.0 mg (0.5%) USUAL DOSAGE: See package insert. Storage: Store upright at 15°-25° C (59°-77° F). KEEP OUT OF REACH OF CHILDREN. US Patent No. 5,800,807	
FOR OPHTHALMIC USE ONLY.	BAUSCH + LOMB		
LOTEMAX[®]	LOTEMAX[®]		
Bausch & Lomb Incorporated Tampa, Florida 33637 ©Bausch & Lomb Incorporated	loteprednol etabonate ophthalmic gel 0.5%		
9239300 AB50307	Sterile Rx Only 5 g		

9239300

Trade Carton – 5g/10 mL bottle:

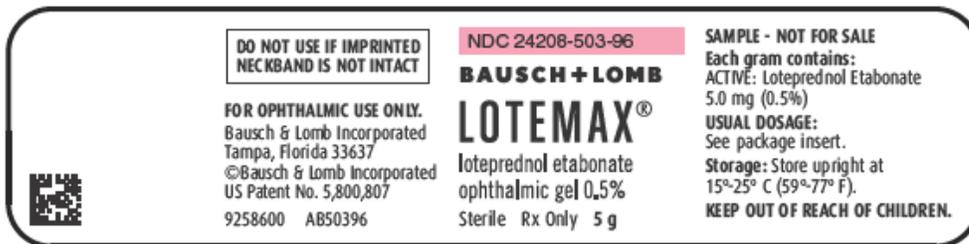


Sample Container Label – 0.5g/4 mL bottle:



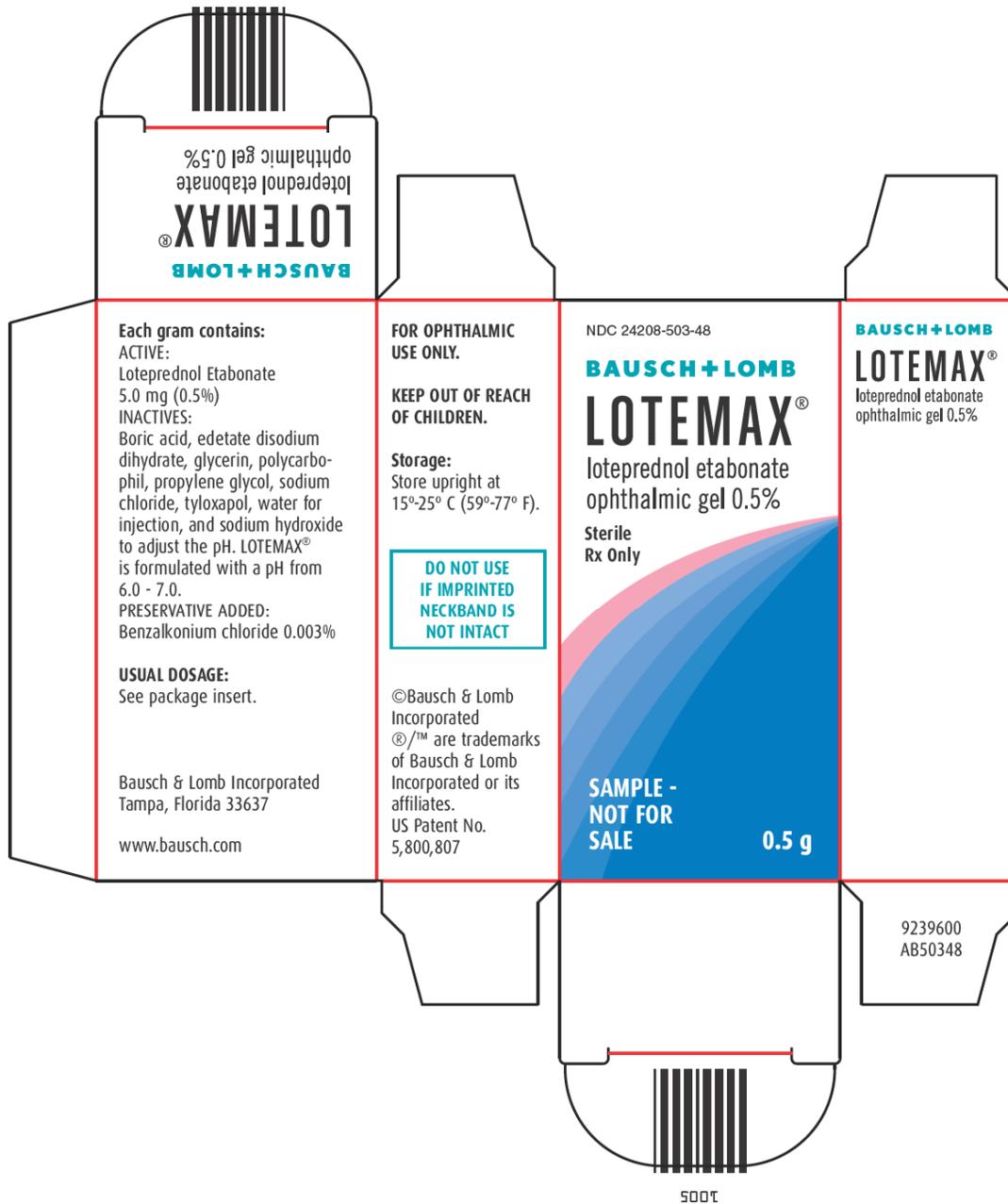
9239700

Sample Container Label – 5g/10 mL bottle :



9258600

Sample Carton – 0.5g/4 mL bottle:



Sample Carton – 5g/10 mL bottle:

