

PRODUCT INFORMATION

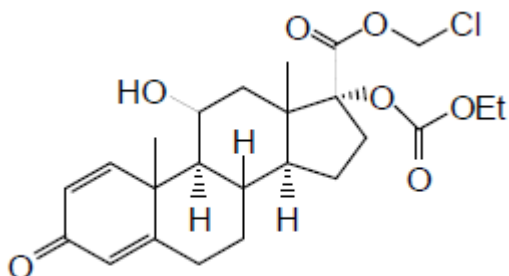
Lotemax[®]

loteprednol etabonate 0.5% eye drops suspension

Name of the medicine

Name: loteprednol etabonate

Chemical structure:



CAS Registry Number: 82034-46-6

Description

Loteprednol etabonate is a white to off-white powder. The chemical name for loteprednol etabonate is chloromethyl 17 α -[(ethoxycarbonyl)oxy]-11 β -hydroxy-3-oxoandrost-1,4-diene-17 β -carboxylate. The empirical formula is C₂₄H₃₁ClO₇ and its molecular weight is 466.96.

Lotemax is a topical anti-inflammatory corticosteroid for ophthalmic use. It is a sterile, milky white ophthalmic suspension of loteprednol etabonate. The suspension is essentially isotonic with a tonicity of 250 to 310 mOsmol/kg. The pH is adjusted to 5.5 - 5.6.

Each mL of Lotemax contains 5 mg of loteprednol etabonate.

Lotemax contains the following inactive ingredients: benzalkonium chloride 0.01% (preservative), disodium edetate, glycerol, povidone, purified water and tyloxapol. Hydrochloric acid and/or sodium hydroxide may be added to adjust the pH.

Pharmacology

Mechanism of action

Corticosteroids inhibit the inflammatory response to a variety of inciting agents and may delay or slow healing. They inhibit the oedema, fibrin deposition, capillary dilation,

leukocyte migration, capillary proliferation, fibroblast proliferation, deposition of collagen, and scar formation associated with inflammation. There is no generally accepted explanation for the mechanism of action of ocular corticosteroids. However, corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2. Corticosteroids are capable of producing a rise in intraocular pressure.

Loteprednol etabonate is structurally similar to other corticosteroids. However, the number 20 position ketone group is absent. Loteprednol etabonate is synthesised through structural modifications of prednisolone-related compounds so that it will undergo a predictable transformation to an inactive metabolite, which may account for the lower risk of intraocular pressure elevation observed in clinical trials, compared to prednisolone. Loteprednol etabonate is highly lipid soluble which enhances its penetration into cells and its binding at the glucocorticoid receptor.

Pharmacokinetics

The available pharmacokinetic data from *in vivo* and *in vitro* studies indicate that loteprednol etabonate is readily absorbed into ocular tissues, with low systemic exposure following topical ocular administration.

Absorption

Results from a bioavailability study in normal volunteers established that plasma levels of loteprednol etabonate and Δ^1 cortienic acid etabonate (PJ-91), its primary, inactive metabolite, were below the limit of quantitation (1 ng/mL) at all sampling times. The results were obtained following the ocular administration of one drop in each eye of 0.5% loteprednol etabonate eight times daily for 2 days or 4 times daily for 42 days. This study suggests that limited (<1 ng/ml) systemic absorption occurs with Lotemax.

Distribution

Topical ocular administration of Lotemax in humans resulted in measurable loteprednol etabonate concentrations in aqueous humour within 20 minutes after dosing, and concentrations of approximately 3.7 ng/mL were observed at one hour after dosing. Loteprednol etabonate is highly protein bound in plasma, and distributes preferentially into the cellular components of blood.

Metabolism

Loteprednol etabonate is readily metabolised to two inactive metabolites, PJ-90 (Δ^1 -cortienic acid) and PJ-91 (Δ^1 -cortienic acid etabonate). Metabolism occurs locally in ocular tissues, and to the extent that loteprednol etabonate reaches the systemic circulation, likely the liver and other tissues into which it distributes.

Excretion

Following systemic administration to rats, loteprednol etabonate is eliminated primarily via the biliary/faecal route, with most of the dose eliminated in the form of the metabolite, PJ-90.

Clinical trials

Post-Operative Inflammation following cataract surgery

Two double-masked, randomised, placebo controlled, parallel group multicentre trials were conducted to evaluate the safety and efficacy of Lotemax in controlling anterior chamber cell and flare reaction in patients requiring elective cataract removal and posterior chamber intraocular lens (IOL) implantation who, on the day following surgery, exhibited a minimum anterior chamber inflammation (ACI) score (sum of cell and flare reaction) of 3 (moderate, 0 to 9 scale).

Patients with history of intraocular or laser surgery on the eye within the past six months or the presence of any ocular pathology other than the cataract (for example vernal conjunctivitis, glaucoma of any kind, giant papillary conjunctivitis, viral or bacterial conjunctivitis, uveitis, retinopathies) were excluded from the trials.

Patients received Lotemax or placebo four times a day in the operated eye one day after surgery for up to 14 days.

The primary efficacy endpoint was the ACI score (the sum of cell and flare ratings) at the final visit (14 days of treatment). Secondary variables assessed for efficacy included: resolution of cell and flare individually, the magnitude of change in the cell and flare ratings, treatment failure and the Investigator's Global Assessment (IGA) at final visit.

In trial 125, by the final visit (Last Observation Carried Forward [LOCF]), ACI had resolved in 64% (70/109) of patients in the Lotemax group and 29% (33/113) of those in the placebo group ($p < 0.001$) (Table 1).

Table 1: Study # 125: Resolution of ACR

Visit	Treatment Group	N at risk	Resolved		Treatment effect	95% CI	p-Value
			N	%			
2 (Day 2 - 6)	Lotemax	109	16	14.7%			
	Vehicle	111	4	3.6%	11.1%	(3.6%, 18.6%)	0.0043
3 (Day 7 - 12)	Lotemax	102	44	43.1%			
	Vehicle	92	17	18.5%	24.7%	(12.2%, 37.1%)	0.0002
4 (Days 13 - 20)	Lotemax	98	69	70.4%			
	Vehicle	76	30	39.5%	30.9%	(16.7%, 45.2%)	< 0.0001
Final visit (LOCF)	Lotemax	109	70	64.2%			
	Vehicle	113	33	29.2%	35.0%	(22.7%, 47.3%)	< 0.0001

NOTE: N at risk is the number of subjects with a score > 0 at baseline and a valid on-treatment evaluation for the visit. LOCF is the last valid on-treatment observation, carried forward. Resolved is the number and percentage of subjects for whom the score was 0 at the endpoint. Treatment effect is the difference between treatments in resolution rates (Lotemax - vehicle) with investigators pooled. Positive treatment effects indicate that Lotemax is favored over placebo for resolution rate. P-value is from the Pearson chi-squared test for independence of treatment assignment and resolution.

The resolution rate and mean change from baseline of the individual components of ACI (cell and flare), as well as other signs and symptoms, were better in the Lotemax group. The treatment failure rate and the time course of failures were lower in the Lotemax group; the differences were clinically meaningful and statistically significant ($p < 0.001$). Three patients in the Lotemax group had an intraocular pressure elevation of ≥ 10 mm Hg over the preoperative screening value at one or more visits.

In study 127, the proportion of patients with ACI resolved by the final visit [LOCF] was 55% (56/102) in the Lotemax group and 28% (28/100) in the placebo group ($p < 0.001$) (Table 2).

Table 2: Study # 127: Resolution of ACR

Visit	Treatment Group	N at risk	Resolved		Treatment effect	95% CI	p value
			N	%			
2 (Day 2-6)	Lotemax	102	10	9.8%			
	vehicle	100	9	9.0%	0.8%	(-7.2%, 8.9%)	0.8448
3 (Day 7-12)	Lotemax	96	33	34.4%			
	vehicle	83	14	16.9%	17.5%	(5.1%, 30%)	0.0079
4 (Days 13 - 20)	Lotemax	93	54	58.1%			
	vehicle	70	27	38.6%	19.5%	(4.3%, 34.7%)	0.0137
Final visit (LOCF)	Lotemax	102	56	54.9%			
	vehicle	100	28	28.0%	26.9%	(13.8%, 40.0%)	0.0001

N at risk is the number of subjects with a score > 0 at baseline and a valid on-treatment evaluation for the visit. LOCF is the last valid on-treatment observation, carried forward. Resolved is the proportion of subjects at risk for whom the score was 0 at the endpoint. Treatment effect is the difference between treatments in resolution rates (Lotemax - vehicle) with Investigators pooled. Positive treatment effects indicate that Lotemax is favored over vehicle for resolution rate. P-value is from the Pearson chi-squared test for independence of treatment assignment and resolution.

In both trials by the final visit (LOCF), the ACI had resolved in a larger proportion of patients treated with Lotemax compared to placebo ($p < 0.001$).

For all the individual components of ACI (cell and flare), as well as other signs and symptoms, the resolution rate and mean change from baseline favoured Lotemax.

Expanding the efficacy criterion to include patients with mild inflammation at final visit, the efficacy of Lotemax was 93% (95/102), in contrast to 65% (65/100) for placebo. The difference in the treatment failure rates, as well the difference in the time-course of failures was both clinically meaningful and statistically significant, in favour of Lotemax ($p < 0.001$). Both treatments were well tolerated. No clinically significant elevations in intraocular pressure (≥ 10 mm Hg) were seen in the Lotemax treatment group in this trial.

Giant Papillary Conjunctivitis (GPC)

Three multicentre, double-masked, parallel-group, placebo-controlled studies (Studies 106, 107, 108) were conducted to evaluate the safety and efficacy of Lotemax in the treatment of GPC associated with wearing contact lenses.

The test medication, Lotemax or placebo, was administered four times a day for 28 days (Study 106) or for 42 days (Study 107 and Study 108).

Study 106 was a multicentre, randomised, double-masked, placebo-controlled, parallel-group comparison of Lotemax and placebo in subjects with bilateral GPC. Subjects instilled one drop of the test medication into each eye four times a day for four weeks. A total of 110 subjects (Lotemax = 55; placebo = 55) completed the study. Subjects receiving Lotemax demonstrated a significant reduction in the primary ocular sign of GPC (papillae, $p < 0.001$) and were rated better in the IGA ($p = 0.017$). Lotemax did not elevate IOP during the study and was clinically effective for the treatment of GPC.

There was no significant improvement in the other primary efficacy endpoints of discharge, dryness and itching. Although the IGA showed significant improvement, there was no significant difference between LE and placebo in Patient's global assessment of their condition.

Study 107 was a randomised, double-masked, placebo-controlled, parallel-group comparison of the safety and efficacy of Lotemax versus placebo in reducing the ocular signs and symptoms accompanying contact lens-associated GPC. A total of 223 adults with contact lens associated GPC received study medication as one drop, four times a day for six weeks.

Papillae, itching, contact lens intolerance, other signs and symptoms of GPC (0-3 or 0-4 grading scales), and IOP were measured. In these studies, subjects were allowed to wear their contact lenses. This decision was partially based upon the preference of myopic subjects not to return to spectacle correction, even with the presence of an inflammatory eye disorder.

The proportion of subjects treated with Lotemax who at final visit demonstrated an improvement in papillae of at least one grade (78%, 85/109) was significantly greater than the proportion of those treated with placebo (51%, 56/110; $p < 0.001$). A treatment difference favouring Lotemax was seen with improvement in itching (95% [104/109] vs. 81% [89/110]; $p = 0.001$) and lens intolerance (87% [95/109] vs 77%, [85/110]; $p = 0.053$).

Table 3: Study #P-5604-107: Summary of Efficacy

	% Responders ¹			Mean AUC ² (Unit-Days)		
	Lotemax	Vehicle	p	Lotemax	Vehicle	p
Papillae	78	51	<0.001	-3.14	-17.1	<0.001
Itching	95	81	0.001	-76.8	-58.7	0.001
Lens Intolerance	87	77	0.053	-55.3	-41.4	<0.001

¹ Final Visit – Improvement over baseline of one or more units

² Negative Number – smaller number indicates greater effect.

Eight of 109 subjects (7%, all treated with Lotemax) had an IOP increase of ≥ 10 mm Hg on at least one visit during treatment. After discontinuation of Lotemax, IOP returned to normal levels.

Study 108 was a randomised, double-masked, placebo-controlled, parallel-group comparison of Lotemax versus placebo for reducing the ocular signs and symptoms accompanying contact lens associated GPC. A total of 220 adults were treated four times a day for six weeks. Papillae, itching, lens intolerance, as well as other signs and symptoms of GPC (0-3 or 0-4 point severity scales), and IOP were measured. The proportion of subjects treated with Lotemax demonstrating an improvement in papillae of at least one grade was significantly greater than those treated with placebo (75% [83/111] vs 50% [55/109], $p < 0.001$). A treatment difference favouring Lotemax was also seen with itching (92% [102/111] vs 76% [83/109], $p < 0.001$) and lens intolerance (84% [93/111] vs 66% [72/109], $p < 0.002$).

Table 4: Study #P-5604-108: Summary of Efficacy

	% Responders ¹			Mean AUC ² (Unit-Days)		
	<i>Lotemax</i>	<i>Vehicle</i>	<i>p</i>	<i>Lotemax</i>	<i>Vehicle</i>	<i>p</i>
Papillae	75	50	<0.001	-38.1	-16.6	<0.001
Itching	92	76	0.001	-73.4	-44.1	<0.001
Lens Intolerance	84	66	0.002	-53.0	-38.8	0.001

¹ Final Visit

² Negative Number – smaller number indicates greater effect.

Three subjects (all on Lotemax) had an IOP elevation of ≥ 10 mm Hg from baseline on at least one on-treatment visit.

Indications

Lotemax is indicated for:

- treatment of post-operative inflammation following cataract surgery
- treatment of steroid responsive inflammatory conditions of contact lens associated giant papillary conjunctivitis (GPC).

Contraindications

Lotemax 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.

Lotemax is also contraindicated in individuals with known or suspected hypersensitivity to loteprednol etabonate or any of the excipients of this preparation and to other corticosteroids.

Precautions

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision, and in posterior subcapsular cataract formation.

Steroids should be used with caution in the presence of glaucoma.

Prolonged use of corticosteroids may suppress the host response and may increase the possibility of secondary ocular infections. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids.

In acute purulent conditions of the eye, steroids may mask infection or enhance existing infection.

The use of steroids after cataract surgery may delay healing.

If signs and symptoms fail to improve after two days, the patient should be re-evaluated.

If this product is used for 10 days or longer, intraocular pressure should be monitored.

Formulations with benzalkonium chloride should be used with caution in soft contact lens wearers.

Effects on Fertility

The effects of Lotemax on sexual function and reproduction have not been studied in humans. Treatment of male and female rats with oral doses up to 50 mg/kg/day and 25 mg/kg/day of loteprednol etabonate, respectively, (approximately 80 and 40 times the maximum clinical dose, respectively, based on body surface area) prior to and during mating did not impair fertility in either gender.

Use in pregnancy

Category B3

Loteprednol etabonate, like other corticosteroids, has been shown to be teratogenic in laboratory animal species. In rats, oral treatment during organogenesis resulted in malformations (cleft palate and umbilical hernia), decreased fetal body weight and retardation of skeletal ossification at ≥ 50 mg/kg/day, and increased post-implantation loss at 100 mg/kg/day; maternal toxicity (significantly reduced body weight gain during treatment) was observed at ≥ 5 mg/kg/day. Oral administration at a dose of 3 mg/kg/day to rabbits during organogenesis caused malformations (meningocele), limb flexure, decreased fetal weight and retarded ossification, occurring in the absence of maternal toxicity. The no-observed-effect-level (NOEL) for these embryofetal effects was 5 mg/kg/day in rats and 0.5 mg/kg/day in rabbits.

Oral administration of loteprednol etabonate to female rats from the start of the fetal period through to the end of lactation gave rise to decreased pup birth weight at ≥ 5 mg/kg/day and decreased growth, reduced survival and retarded development in the offspring during lactation at 50 mg/kg/day. Treatment at these dose levels was maternotoxic (significantly decreased body weight gain). The NOEL for these effects was 0.5 mg/kg/day. Loteprednol etabonate has no significant 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. Loteprednol etabonate should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Use in lactation

Caution should be exercised when Lotemax is administered to a nursing mother as studies in lactating women have not been conducted. Adverse effects have been observed in the offspring of rats treated orally with loteprednol etabonate during gestation and lactation (see Use in Pregnancy). It is not known whether topical ophthalmic administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk.

Use in children

Lotemax should not be used in children. The safety and efficacy of Lotemax has not been studied in children.

Use in the elderly

No differences in efficacy or adverse events profile have been observed between the elderly and younger patients. Therefore, no dosage adjustment is required for elderly patients.

Genotoxicity

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.

Carcinogenicity

Long-term animal studies have not been conducted to evaluate the carcinogenic potential of loteprednol etabonate.

Effects on laboratory tests

None.

Interactions with other medicines

No interactions are anticipated in humans, since systemic concentrations of loteprednol etabonate are extremely low following ocular dosing. Therefore, specific drug interaction studies have not been performed with loteprednol etabonate.

Adverse effects

Very commonly reported ocular adverse events (occurring in >10% of subjects receiving LE) in clinical trials (Studies 106, 107, 108, 125, 127, 122/1221, 126) were abnormal

vision and IOP increased. Studies 122/1221 and 126 are studies for Acute Anterior Uveitis and are not described in the Clinical Trials section.

There was no very commonly reported non-ocular adverse in subjects receiving LE.

Commonly reported adverse events (occurring in $\geq 1\%$ to $<10\%$ of subjects) were itching eye, photophobia, epiphora, injection (pooled), discomfort eye, foreign body sensation, discharge eye, dry eye, eye pain, uveitis, cells anterior chamber, burning/stinging eye, erythema eyelids, keratic precipitate, flare anterior chamber, papilla, inflammation anterior chamber, ciliary flush, corneal abnormality.

Commonly reported non-ocular adverse events included headache and infection.

Tabulated adverse events of incidence $>1\%$ from clinical trials (Studies 106, 107, 108, 122/1221, 125, 126 and 127) comparing loteprednol etabonate to vehicle/comparator are provided in Table 8.

**Table 8 Adverse Events $>1\%$ in loteprednol etabonate and placebo/comparator groups
from Clinical Studies 106, 107, 108, 122/1221, 125, 126 and 127**

Adverse Events	LE 0.5% (n=656)	Placebo (n=497)	Prednisolone Acetate (n=170)
<i>Eye Disorders</i>	%	%	%
Abnormal vision	15.4	16.7	21.2
IOP increased	10.2	3.4	23.5
Itching eye	9.0	14.3	4.7
Photophobia	7.6	21.9	1.8
Epiphora	7.5	15.5	1.2
Injection (pooled)	6.4	20.5	0.6
Discomfort eye	6.3	10.9	4.7
Foreign body sensation	6.1	9.3	0.0
Discharge eye	5.5	8.2	1.2
Dry eye	4.4	4.8	4.7
Eye pain	3.5	11.1	3.5
Uveitis	2.7	1.6	2.4
Cells anterior chamber	2.6	4.0	1.8
Burning/stinging eye	2.1	2.8	0.6
Erythema eyelids	2.0	6.4	0.0
Keratic precipitate	2.0	0.0	2.9
Flare anterior chamber	1.7	4.6	1.8
Papilla	1.2	3.6	0.0
Inflammation anterior chamber	1.2	2.8	0.0
Ciliary flush	1.1	3.4	0.6
Corneal abnormality	1.1	0.8	1.2
Iritis	0.9	1.6	1.8
Vision, blurred	0.9	1.6	1.8
Oedema, corneal	0.8	3.4	0.6
Eye disorder	0.8	1.8	0.6
Keratoconjunctivitis	0.8	0.4	1.8
Conjunctivitis	0.6	1.0	0.0

Adverse Events	LE 0.5% (n=656)	Placebo (n=497)	Prednisolone Acetate (n=170)
Chemosis	0.5	1.8	0.6
Papillae increased	0.5	1.2	0.0
<i>Nervous System Disorder</i>			
Headache	7.6	12.5	4.7
<i>Infections and Infestations</i>			
Infections	2.0	2.4	0.6
<i>Respiratory, thoracic and mediastinal disorders</i>			
Rhinitis	0.9	1.0	1.8
<i>Immune System Disorder</i>			
Allergic reaction	0.8	2.6	0.6

Uncommon ocular adverse events (occurring $\geq 0.1\%$ to $\leq 1\%$ of subjects) included iritis, vision blurred, lacrimation disorder, corneal oedema, eye disorder, keratoconjunctivitis, conjunctivitis, corneal lesion, eyelid abnormality, tearing, chemosis, papillae increased, macular oedema, keratitis, mucus, redness, contact lens intolerance, irritation eye, synechia anterior chamber, vitreous disorder, sticky eyes, hyphaema, limbal staining, accommodation abnormality, conjunctival hemorrhage, mydriasis, amblyopia, ophthalmitis, papilledema, vasculitis, vitreous strands, vitritis, fluorescein staining, swollen tear duct, corneal abrasion, tired and puffy eyes.

Uncommon non-ocular adverse events included rhinitis, pharyngitis, allergic reaction, migraine, facial edema, fever, gastritis, nausea and vomiting.

In controlled randomised studies of patients treated for 28 days or longer with loteprednol etabonate, the percentage of patients with an increase in intraocular pressure greater than 10 mm Hg was 2% (15/901) for loteprednol etabonate, 7% (11/164) for 1% prednisolone acetate, and 0.5% (3/583) for placebo.

Post-Marketing events:

The following adverse reactions are classified according to the following convention (% of total adverse events reported for loteprednol etabonate):

- Very common ($\geq 10\%$)
- Common ($\geq 1\%$ to $< 10\%$)
- Uncommon ($\geq 0.1\%$ to $< 1\%$)
- Rare ($\geq 0.01\%$ to $< 0.1\%$)
- Very rare ($\geq 0.001\%$ to $< 0.01\%$)
- Not known (cannot be estimated from the available data)

According to system organ classes, the following adverse reactions have been reported during post-marketing experience. The percentages are based on the total number of adverse events reported in post-marketing data.

Ear and labyrinth disorders:

Uncommon - hypoacusis, tinnitus and vertigo

Eye disorders:

Common - corneal deposits, corneal infiltrates, corneal oedema, corneal striae, dry eye, eye irritation, eye pain, eye pruritis, eye swelling, foreign body sensation in eyes, lacrimation increased, ocular discomfort, ocular hyperaemia, periorbital edema, punctate keratitis, visual acuity reduced and vision blurred.

Uncommon – anterior chamber cell, anterior chamber fibrin, aqueous fibrin, abnormal sensation in eye, atrophy of globe, cataract, conjunctival hyperemia, conjunctivitis, corneal opacity, corneal scar, corneal striae, eye discharge, eye inflammation, eyelid oedema, keratitis, glaucoma, halo vision, iritis, ulcerative keratitis, visual acuity reduced and visual impairment

Gastrointestinal disorders:

Uncommon: nausea, and tooth ache

General disorders and administrative site conditions:

Common: condition aggravated, drug ineffective and medication residue

Uncommon: drug ineffective for unapproved indication, impaired healing, inflammation, malaise, and pain

Immune system disorders:

Common: drug hypersensitivity, hypersensitivity

Infections and infestations:

Uncommon: endophthalmitis and sinusitis

Injury, poisoning and procedural complications:

Common: corneal flap complication, diffuse lamellar keratitis

Uncommon: corneal abrasion, foreign body in eye, incorrect drug administration duration, medication error, and toxicity to various agents

Investigations:

Common: intraocular pressure increased

Uncommon: blood glucose increase,

Metabolism and nutrition disorders:

Uncommon: decreased appetite

Musculoskeletal and connective tissue disorders:

Rare: back pain, muscle spasms, muscle twitching

Nervous system disorders:

Common: headache

Uncommon: dizziness, facial spasms, migraine, sinus headache and visual field defect

Psychiatric Disorder:

Uncommon: Insomnia, anxiety

Respiratory, thoracic and mediastinal disorders:

Uncommon: oropharyngeal pain and dyspnoea

Skin and subcutaneous tissue disorders:

Uncommon: alopecia, erythema, madarosis, photosensitivity reaction, pruritis generalised, skin burning sensation, swelling face

Surgical and medical procedure:

Common: Off label use.

Dosage and administration

SHAKE VIGOROUSLY BEFORE USING.

For individual patient use only

If signs and symptoms fail to improve after two days, the patient should be re-evaluated (See **Precautions**).

Post-Operative Inflammation following cataract surgery

Apply one to two drops of Lotemax into the conjunctival sac of the operated eye(s) four times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the post-operative period.

Steroid responsive inflammatory conditions of contact lens associated giant papillary conjunctivitis (GPC)

Apply one to two drops of Lotemax into the conjunctival sac of the affected eye(s) four times daily.

Systemic absorption of Lotemax may be reduced by compressing the lacrimal sac at the medial canthus for a minute during and following the instillation of the drops (this blocks the passage of the drops via the naso-lacrimal duct to the wide absorptive area of the nasal and pharyngeal mucosa).

Overdosage

Overdose is unlikely to occur after ocular administration. If overdose occurs, treatment should be symptomatic. Contact the Poisons Information Centre on 131126 for advice on management.

Presentation and storage conditions

Presentation

Lotemax loteprednol etabonate 0.5% eye drops suspension is supplied as a sterile suspension in a white low density polyethylene (LDPE) bottle with a controlled dropper tip and polypropylene cap. Tamper evidence is provided with a shrink band around the cap and neck area of the bottle.

**Attachment 1: Product information for AusPAR Lotemax loteprednol etabonate Bausch & Lomb
PM- PM-2012-03141-1-5 Date of Finalisation 17 April 2014. This Product Information was approved
at the time this AusPAR was published.**

Lotemax loteprednol etabonate 0.5% eye drops suspension is available in the following pack sizes: 2.5ml (sample pack), 5ml, 10ml and 15ml.

Storage Conditions

Store below 25°C.

Do not freeze.

Store in an upright position.

Discard container four weeks after opening.

Name and address of sponsor

Bausch & Lomb (Australia) Pty Ltd
G/F 16 Giffnock Avenue,
Macquarie Park
NSW 2113

Poison schedule of the medicine

S4 – Prescription Only Medicine

Date of first inclusion in the Australian Register of Therapeutic Goods (ARTG)

16 Jan 2014