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Cataract & Refractive Surgery Today Advanced Ocular Care

Postsurgical Insights

for Managing Ocular Inflammation and Pain With Lotemax Gel Following Ocular Surgery

INDICATION

LOTEMAX® GEL (loteprednol etabonate ophthalmic gel) 0.5% is indicated for the treatment of post-operative inflammation and pain following ocular surgery.

IMPORTANT SAFETY INFORMATION ABOUT LOTEMAX® GEL

- LOTEMAX® GEL 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.
- 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.
- Use of corticosteroids may result in posterior subcapsular cataract formation.
- Use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation and occurrence of perforations in those with diseases causing corneal and scleral thinning. 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, and, where appropriate, fluorescein staining.
- 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.
- Use 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 exacerbate the severity of many viral infections of the eye (including herpes simplex).
- 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.
- Patients should not wear contact lenses when using LOTEMAX® GEL.
- The most common ocular adverse drug reactions reported were anterior chamber inflammation (5%), eye pain (2%) and foreign body sensation (2%).

Please see Full Prescribing Information for LOTEMAX® GEL on pages 11-12.

LOTEMAX® GEL
loteprednol etabonate
ophthalmic gel 0.5%

Legacy and Benefits of Lotemax Gel

A look at the history and safety profile of Lotemax Gel for the treatment of inflammation and pain following ocular surgery.

HERITAGE OF THE MOLECULE

The loteprednol etabonate molecule has been extensively studied,[1] with demonstrated postoperative control of inflammation and pain following ocular surgery as well as a low incidence of IOP elevation.[2] It has been on the market for 15 years, has been used in thousands of patients, and has evolved to include suspension, ointment, and gel formulations.

"The history of loteprednol etabonate, both in terms of clinical studies and in terms of clinical use, is important to me because I know that what I am giving to my patients to control their inflammation and pain after ocular surgery is a product with a demonstrated efficacy and safety profile," says Marguerite McDonald, MD.

CLINICAL EXPERIENCE

It is widely known that prolonged use of corticosteroids may result in elevated IOP. In phase 3 trials, Lotemax Gel (loteprednol etabonate ophthalmic gel 0.5%) showed an incidence of increased IOP similar to vehicle, as far out as day 14. Mean IOP was similar between treatment groups and consistently lower than baseline (Figure 1).[2]

In phase 3 trials, Lotemax Gel also demonstrated statistically significant inflammation and pain control. More patients achieved complete resolution of anterior chamber cells and grade 0 pain with Lotemax Gel (n = 409) versus vehicle (n = 404) at day 8 (anterior chamber cell resolution: 31% vs 15%, $P < 0.001$; grade 0 pain: 74% vs 44%, $P < 0.001$), with continued efficacy at day 15 (anterior chamber cells resolution: 53% vs 26%, $P < 0.001$; grade 0 pain: 77% vs 41%, $P < 0.001$).[2]

"My clinical experience with Lotemax Gel aligns with these data," says John D. Sheppard, MD. "Lotemax Gel provides the inflammation control and pain control I am looking for following ocular surgery."

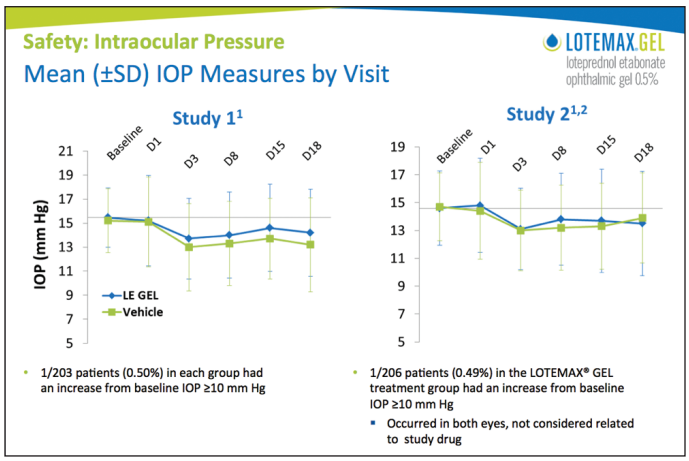

Figure 1. Mean IOP was similar between treatment groups and consistently lower than baseline.[2] If Lotemax Gel is used for 10 days or longer, IOP should be monitored.

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Please see additional Important Safety Information on page 1.

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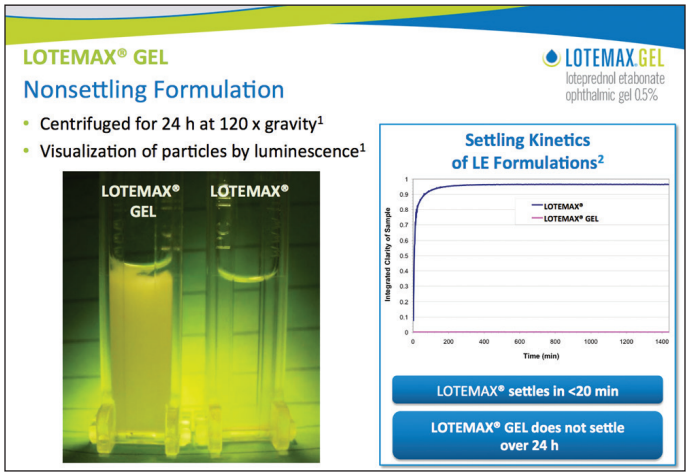

Figure 2. Lotemax Gel's nonsettling formulation did not settle over 24 hours.

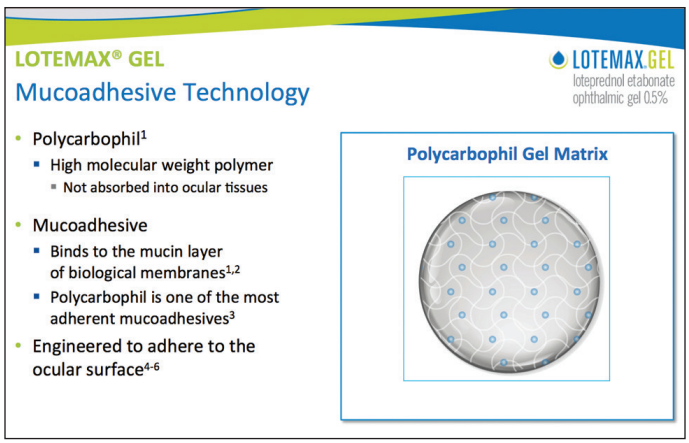

Figure 3. Lotemax Gel has mucoadhesive technology that is engineered to adhere to the ocular surface.

FEATURES OF GEL FORMULATION

There is no one patient type for using Lotemax Gel. It is a good option for inflammation and pain following any ocular surgery, including refractive, cataract, and corneal surgeries.[2,3]

The gel formulation of Lotemax provides a consistent concentration of loteprednol in every drop.[4] In one study (n = 100), 63% of patients did not shake an ophthalmic suspension medication despite a labeled direction to shake.[5] Lotemax Gel was not used in this study. Lotemax Gel's nonsettling formulation was compared to the suspension formulation of loteprednol etabonate (centrifuging for 24 hours at 120x gravity); the results showed that the suspension formulation of loteprednol etabonate settled in less than 20 minutes, whereas Lotemax Gel did not settle over 24 hours (Figure 2).[4]

"I like knowing that when my patients are at home, administering their own drops, they are getting a consistent concentration in every drop to control their pain and inflammation around the clock," says Christopher E. Starr, MD. "It is one less thing patients have to think about when following their postsurgical protocol."

Lotemax Gel has mucoadhesive technology that is engineered to adhere to the ocular surface (Figure 3). Adaptive viscosity technology allows it to be a gel at rest and transforms it into a viscous liquid under shear stress (ie, blinking) and due to electrolytes in the tear fluid, making it more than 10x more viscous than the suspension formulation of loteprednol etabonate.[6] It also has a lower preservative concentration (30 ppm benzalkonium chloride) than the suspension formulation of loteprednol etabonate; it includes a proprietary blend of moisturizers (glycerin, propylene glycol); and it is close to the physiologic pH of tear fluid (buffer keeps pH centered at 6.5).[3]

NO GENERIC SUBSTITUTION

Ocular surgery, including cataract surgery, is an investment.

IMPORTANT SAFETY INFORMATION ABOUT LOTEMAX® GEL (CONTINUED)

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Please see additional Important Safety Information on page 1.

Postsurgical management is important. Lotemax Gel has a proven efficacy and safety profile in clinical trials.[2] There is no generic substitute for it.

"I always encourage my patients to fill their prescriptions exactly as I have written them, and my office staff is trained to let pharmacies know to follow my prescriptions as written," says Karl G. Stonecipher, MD.

If patients need help paying for their prescription, Bausch + Lomb provides copay programs that may help them get the medicines they need. Final costs will depend on insurance coverage, but there are multiple programs in place. ■

Marguerite McDonald, MD, is a cornea/refractive specialist with Ophthalmic Consultants of Long Island, New York. She is also clinical professor of ophthalmology at NYU Langone Medical Center, New York, and Tulane University Health Sciences Center, New Orleans. Dr. McDonald is a consultant for Bausch + Lomb. She may be reached at margueritemcdmd@aol.com.

John D. Sheppard, MD, MMSc, is a professor of ophthalmology, microbiology & immunology, clinical director of the Thomas R. Lee Center for Ocular Pharmacology, and ophthalmology residency research director at the Eastern Virginia Medical School in Norfolk, Virginia. He is also the president of Virginia Eye Consultants and the medical director of the Lions Eye Bank of Eastern Virginia. He is a consultant to Bausch + Lomb. Dr. Sheppard may be reached at docshep@hotmail.com.

Christopher E. Starr, MD, is associate professor of ophthalmology, director of the Refractive Surgery Service, director of ophthalmic education, and director of the Cornea, Cataract, and Refractive Surgery Fellowship at Weill Cornell Medical College. He is a consultant to Allergan, Bausch + Lomb, Rapid Pathogen Screening, Shire, and TearLab. Dr. Starr can be reached at cestarr@med.cornell.edu.

Karl G. Stonecipher, MD, is director of refractive surgery at TLC in Greensboro, North Carolina, and clinical associate professor of ophthalmology at the University of North Carolina at Chapel Hill. He is a consultant to and speaker for and has received grant support and travel reimbursement from Abbott Medical Optics and Alcon Laboratories. Dr. Stonecipher may be reached at stonenc@aol.com.

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A Treatment Option Following Any Ocular Surgery

Physicians share their experiences using Lotemax Gel for postoperative control of inflammation and pain following ocular surgery, including LASIK, pterygium, MIGS, and PRK.

CASE 1
LASIK After Unsatisfactory Cataract Surgery With Multifocal IOL

By Douglas Katsev, MD

A 63-year-old man presented to our clinic dissatisfied with his visual acuity. He had undergone bilateral cataract surgery 4 months prior and had received a refractive multifocal IOL. Having invested in a premium IOL, and hoping to limit his dependence on spectacles, the patient remained not quite satisfied with his vision after cataract surgery.

At the time of his visit, the patient's refraction was 0.75 D with 0.75 D of against-the-rule astigmatism in both eyes. In addition, this patient complained of occasional ocular dryness symptoms, particularly after prolonged tasks like reading and working at the computer. At the slit lamp, a lowered tear meniscus and shortened tear breakup time were noted. His eyelids appeared normal without significant infection, scurf, or capped glands. However, diagnostic gland expression revealed slightly opaque meibum.

In order to give this patient the quality of distance and near vision he desired, we discussed the option of LASIK, which he strongly favored. As part of this conversation, I let the patient know that, without some preoperative intervention, performing the LASIK procedure might temporarily exacerbate his mild dry eye and possibly affect not only his comfort but also the quality of his vision. With this in mind, I prescribed preservative-free artificial tears for him to use as needed for a few weeks leading up to his surgery. When the patient presented on the day of surgery, he reported symptomatic relief from the artificial tears. His tear film and ocular surface looked normal. Therefore, I was comfortable confirming his measurements and proceeded as planned.

I identified the LASIK flap's edge and lifted it with the superior hinge. With the flap thus protected and the stromal bed dry, I obtained centration and performed the hyperopic correction (Figure). I then replaced the flap and irrigated the cornea.

For all my patients, my top priorities in the immediate postoperative period are to control any inflammation and maintain the stability of the patient's tear film. I instructed this patient to continue with the preservative-free artificial tears. To control postoperative pain and inflammation, I prescribed Lotemax Gel (loteprednol etabonate ophthalmic gel 0.5%) four times daily for 14 days

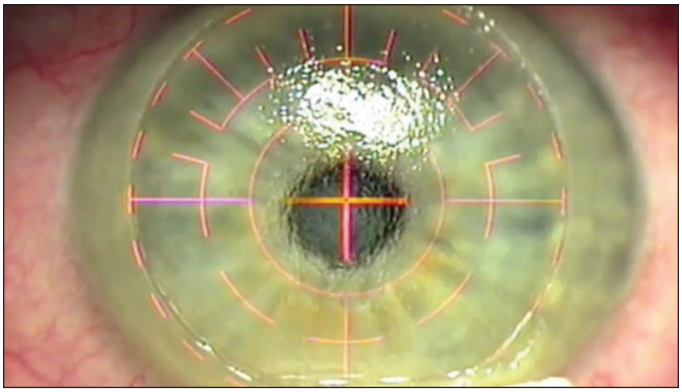

Figure. Obtaining centration and performing the hyperopic correction during LASIK surgery.

following his surgery. Lotemax Gel has a demonstrated efficacy profile, including a low risk of a significant IOP increase, and it was a suitable choice for this individual, as it is for many of my patients after LASIK.[1] If Lotemax Gel is used for 10 days or longer, IOP should be monitored. The formulation of Lotemax Gel provides a consistent delivery of the drug with every dose, and it is designed to remain on the surface of the eye where it is needed.[2] Lotemax Gel also contains the demulcents propylene glycol and glycerin. Lotemax Gel is indicated for postoperative inflammation and pain control following ocular surgery.[1] Lotemax Gel should not be used intraoperatively beneath the LASIK flap.

I have had a great experience using Lotemax Gel postoperatively for inflammation and pain control in my LASIK patients. Indeed, this patient experienced an excellent visual outcome with a final refraction of -0.25 +0.25 X 90. He seldom has to use glasses, even for reading, and he has referred many new patients to our practice.

Douglas A. Katsev, MD, is in private practice at the Sansum Clinic in Santa Barbara, California. He is a consultant to Bausch + Lomb. Dr. Katsev may be reached at katsev@aol.com.

CASE 2
Primary Pterygium Surgery in a 32-Year-Old Patient

By Barry A. Schechter, MD

A 32-year-old woman presented to our clinic with a primary pterygium on the nasal side of her left eye. She complained of a persistent foreign body sensation and blurred UCVA when compared to her fellow eye.

During surgery, I approach the pterygium with forceps and a syringe of Xylocaine 2% (lidocaine; AstraZeneca) with epinephrine, and I perform the injection just underneath the pterygium to balloon up the fibrotic tissue. Then, using blunt scissors, I remove the pterygium tail. It is very important to preserve yet undermine the conjunctiva and remove as much fibrovascular Tenon tissue as possible to limit recurrence, improve cosmesis, and reduce postoperative inflammation.

Having removed most of the pterygium, I irrigate the surface and avulse the remaining tissue from the limbal area with toothed forceps. I then polish the limbal area with a diamond burr to further reduce the load of remaining fibrovascular tissue. Next, I lightly cauterize the area. Using calipers, I measure the area of the excision site in order to prepare the graft. I dry an area of the superior conjunctival surface and mark the graft area, marking just forward of the superior limbal arcade of vessels in order to harvest stem cells, oversizing it by about 1 millimeter in the lateral and posterior directions to ensure coverage of the bed. Then, once more using Xylocaine 2% with epinephrine I create a small balloon and dissect a very thin graft from the superior bulbar conjunctiva, leaving Tenon tissue behind. Obtaining a thin, slightly oversized graft is helpful to optimize the cosmetic outcome of pterygium surgery.

With blunt scissors and forceps, I free the conjunctival graft, taking care to include the limbal corneal epithelium that contains stem cells. My demarcation line is just in front of the limbal

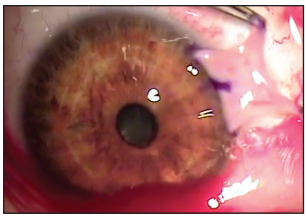

Figure. The surgeon positions the graft during pterygium surgery.

vascular arcade. I consider this step essential to keeping my rate of pterygium recurrence very low because stem cells form the new limbus and act as a barrier to regrowth. I use a crescent blade to complete the dissection into the peripheral cornea, harvesting those stem cells. I place the graft onto the cornea, epithelial side down, align the limbal edge of the graft with the area of the limbus adjacent to the excision site, and I dry the scleral bed. Keeping the graft properly oriented is vital, and we always mark the limbal side of the graft accordingly. Into the subconjunctival space adjacent to the excision area, I tuck a piece of amniotic membrane to aid postoperative healing by inhibiting fibrovascular proliferation, neovascularization, and inflammation. I place the amniotic membrane at the distal edge of the conjunctival bed, the place where recurrence of fibrotic tissue is likely to develop first, which I believe also helps to limit recurrence and gives a nice cosmetic outcome.

My amniotic membrane is in dehydrated form. It is easy to use and cut to the appropriate size, and yet it retains a dense extracellular matrix that hinders fibrovascular growth and activity. To affix the autograft, I use fibrin adhesive. Its two components—thrombin and fibrinogen—mimic natural clot formation when combined. I place a very small amount of thrombin onto the bare sclera, add a small amount of fibrinogen to the underside of the conjunctival graft, and quickly evert the graft to combine them (Figure). Using forceps, I quickly position and squeegee the graft in place, and I pinch the periphery to make sure the edges are sealed. At this stage, I go back to lightly cauterize the donor site. As a final step, I place a bandage contact lens, which helps maintain the patient's comfort by covering the epithelial defect and serves to help keep the graft of limbal stem cells in place during the first postoperative week.

Surgical techniques that induce less postoperative inflammation (for example, the use of fibrin glue rather than sutures) are associated with lower rates of pterygium recurrence.[3] Pharmacologic inflammation control in the postoperative period is also an essential part of pterygium management. For this patient, I prescribed Lotemax Gel (loteprednol etabonate ophthalmic gel 0.5%), dosed four times per day for 14 days. I favor Lotemax Gel in particular for these cases because it offers excellent anti-inflammatory efficacy coupled with a low risk of significant IOP spikes.[1] I routinely see pterygium patients at 1 day, 1 week, and 5 weeks postoperatively. At this patient's 1-day and 1-week visits, her eye looked good, and she was healing well. At 1 week, bandage contact lens use was discontinued, and I instructed her to continue with the postoperative medication regimen.

In pterygium surgery, I find that using advanced technology, such as fibrin glue and prepared amniotic tissue, as well as meticulous surgical technique to harvest limbal stem cells, is important. Lotemax Gel is a good option to treat inflammation and pain in patients following pterygium surgery.

Barry A. Schechter, MD, is director, Department of Cornea and External Diseases, Florida Eye Microsurgical Institute, Boynton Beach, Florida. He serves as a consultant to Abbott Medical Optics and Bausch + Lomb, and he is a member of the speakers board for Omeros. Dr. Schechter can be reached at baschechter@gmail.com.

CASE 3
iStent Implantation in Cataractous Eye With Early Open-Angle Glaucoma

By Inder Paul Singh, MD

In recent years, I have seen a proliferation of options for performing microinvasive glaucoma surgery (MIGS). Most MIGS procedures involve the use of microstent devices, which improve

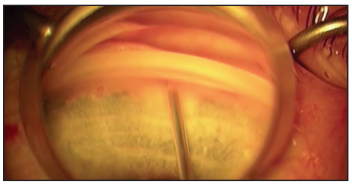

Figure. The surgeon gently taps the snorkel end of the iStent implant to make sure it is in place.

aqueous outflow through a physiologic pathway. MIGS can be successful in patients with mild to moderate glaucoma,[4] and because they spare the conjunctiva, these procedures preserve the tissue for more aggressive filtering surgery as a future treatment option, should it become necessary.

Even as MIGS devices and procedures continue to evolve, outcomes still depend on careful surgical technique and postoperative management. This case involves a 64-year-old woman who presented to my practice complaining of decreased vision, especially at night. An examination revealed significant cataract, and the patient also had glaucoma, which was controlled using two topical IOP-lowering medications. As the patient was motivated to reduce her reliance on eye drops, we discussed the implantation of the iStent Trabecular Micro-Bypass Stent (Glaukos) in conjunction with her cataract surgery.

The first-generation iStent is a 1-mm long, 0.3-mm tall L-shaped titanium implant designed to allow aqueous to flow from anterior chamber directly to Schlemm's canal, bypassing the trabecular meshwork. The iStent is FDA approved for use in conjunction with cataract surgery in patients with mild to moderate open-angle glaucoma. The iStent is typically not implanted as a stand-alone procedure but is performed in conjunction with cataract surgery; the device is inserted into Schlemm's canal via the trabecular meshwork using a preloaded inserter.

This patient made an ideal candidate for the combined procedure, because she had symptomatic cataract and early open-angle glaucoma. She was already on more than one drop to control her IOP and wished to decrease the burden of medication for managing her glaucoma. After I completed the cataract procedure, I was ready to insert the iStent. I added more viscoelastic to deepen the chamber, and I entered the eye through the same clear corneal incision used in the primary procedure. Using a goniolens, I was able to visualize the angle and could see Schwalbe's line, pigmented trabecular meshwork, the scleral spur, and the ciliary body. I approached the upper part of the trabecular meshwork at an angle of 15º, engaged the meshwork tissue, and entered Schlemm's canal. The iStent moved forward into the canal. I released the iStent, and then I used the tip of the inserter to gently tap the snorkel end of the implant to make sure it was properly and securely placed (Figure). The implant fit nicely in the canal. Then, I removed the viscoelastic in the anterior chamber. There was a little reflux of blood in the area where the iStent was implanted. This was a good sign, as it showed me that the iStent is well positioned and already communicating with the venous drainage system. The surgery went well.

For this patient, I used Lotemax Gel (loteprednol etabonate ophthalmic gel 0.5%) the day after surgery four times a day for 14 days. Lotemax Gel is engineered to facilitate residence time on the ocular surface and, in contrast to the suspension formulation of loteprednol etabonate, does not require shaking to ensure dose-to-dose uniformity of drug delivery.[2] Lotemax Gel is indicated for the treatment of postoperative inflammation and pain following ocular surgery. The drug offers a proven safety profile and a low propensity to cause significantly elevated IOP. In phase 3 trials, Lotemax Gel showed an incidence of increased IOP similar to vehicle, as far out as day 14.[1] If Lotemax Gel is used for 10 days or longer, IOP should be monitored. When I removed the cataract and implanted an iStent in this patient's fellow eye, I again began with Lotemax Gel on day 1 after surgery, four times a day for 14 days. The patient experienced an uneventful postoperative course and a rapid visual recovery.

Inder Paul Singh, MD, is a glaucoma specialist at The Eye Centers of Racine and Kenosha in Racine, Wisconsin. He acknowledged no financial interest in the products or companies mentioned herein. Dr. Singh may be reached at ipsingh@amazingeye.com.

CASE 4

PRK: Rapid Epithelial Removal With an "Epi-rhexis" Technique

By Christopher E. Starr, MD

Although LASIK has garnered a reputation for being associated with less pain and faster recovery, I perform mostly advanced surface ablation on my refractive surgery patients. I find modern PRK to be simple and reliable. Visual outcomes are comparable to those with LASIK, and the patient's experience with PRK has vastly improved in the modern era and now really rivals that of patients undergoing LASIK.[5]

I would like to present a clinical case from my practice that illustrates my approach to PRK and perhaps my rationale for using it. A 30-year-old woman presented to my clinic seeking laser vision correction for myopia. Her refractive error was -4.00 D sphere in both eyes. She was intolerant of contact lenses and complained of symptoms consistent with mild dry eye disease. An evaluation revealed central corneal staining and high tear osmolarity. Prior to scheduling surgery, we took steps to optimize the condition of her ocular surface. She was advised to discontinue contact lens wear and wear glasses instead. She was placed on a 30-day regimen for the treatment of dry eyes. On follow-up at 6 weeks, the patient's corneal surface appeared normal and revealed no staining. Her corneal topography and osmolarity were also normal. We were then able to proceed to PRK.

I think sterile technique is essential to the safety and success of any outpatient procedure, including PRK and LASIK. I wear a mask, a cap and gown, and sterile gloves, and I use a sterile drape over the patient's head and lashes. A sterile drape is placed over the joystick and buttons as well before every case. I always make sure to change my gloves in between eyes. To start off, a sponge soaked in topical tetracaine is applied to the cornea, conjunctiva, and lid margin for about 30 seconds. This reduces pain and weakens the corneal epithelium. To further soften the epithelium, alcohol is instilled in a 9-mm well placed against the cornea for about 25 seconds. If alcohol leaks out, the patient will experience more redness and pain postoperatively. Therefore, it is important to hold the well firmly against the cornea, actually retropulsing the eye slightly. Before releasing the ring, I use a sponge to absorb excess alcohol and gently score the epithelium.

Now, I am ready to perform what I call the "epi-rhexis" using a dry Weck-Cel spear (Beaver-Visitec International). I try to remove the epithelium fairly rapidly in one sheet to prevent hydration changes in the stroma. Trying to limit stromal dehydration protects against excessive laser ablation and overcorrection. Ablation is performed using a laser equipped with iris registration and eye-movement tracking for optimal accuracy. In cases of moderate or high myopia, a mitomycin C-dampened sponge is applied to the ablated corneal surface for 12 seconds, and I take care to avoid any exposure to the limbal stem cells. The eye is then irrigated with two bottles of chilled balanced salt solution. One drop of prednisolone acetate is instilled; then the epithelial edge is visualized, any scrolled edges are flattened, and any alcohol-soaked tags are removed. I then apply a bandage contact lens. I want it to fit relatively tightly to facilitate healing and minimize postoperative pain.

The procedure is then repeated on the fellow eye. Tetracaine is applied to the cornea, conjunctiva, and lid margin, alcohol is placed in the well, excess is absorbed, and the epithelium is scored. Epithelium is then removed using a dry Weck-Cel spear. Again, I am aiming for rapid and consistent epithelial removal. Laser ablation is performed, mitomycin C is applied, and the eye is irrigated with chilled balanced salt solution. A drop of corticosteroid is then instilled. Imperfections along the epithelial edge are cleaned up, and a bandage contact lens is applied.

My standard practice for postoperative care includes short-term topical corticosteroids and long-term topical cyclosporine for about 6 months. Pain control is achieved by oral nonsteroidal anti-inflammatory agents, chilled preservative-free artificial tears, and cold compresses. In my practice, I have not found it necessary to prescribe oral corticosteroids, oral narcotics, neuroleptic

TABLE: PRK RESULTS, VISUAL OUTCOMES

	UCVA Both Eyes, Mean (range)
Immediately postprocedure	20/23 (20/15 to 20/30)
POD 1	20/20 (20/15 to 20/30)
POD 4	20/28.5 (20/15 to 20/40)
POM 1	20/16 OU (20/15 to 20/25 OU)
POM 6	20/15 in 100% in each eye

N = 10. Abbreviations: POD, postoperative day; POM, postoperative month.

agents, topical anesthetics, or comfort drops. I prescribe two oral supplements in the week following surgery: ascorbic acid (vitamin C) and omega-3 essential fatty acids. Ascorbic acid is used to prevent late-onset corneal haze associated with exposure to solar ultraviolet radiation. Omega-3 fatty acids have been associated with improved speed of healing, tear breakup time, and visual acuity recovery following PRK.[6]

The patient was placed on Lotemax Gel (loteprednol etabonate ophthalmic gel 0.5%) four times daily for 14 days following surgery. Lotemax Gel reduces pain and inflammation following ocular surgery.[1] I find it to be a good treatment option for patients undergoing mild to moderate refractive error correction with PRK. This is important for patients who chose to have PRK with me rather than LASIK somewhere else. In a wholly elective surgery like PRK, where patients have extremely high expectations, I need to have faith in the agents I prescribe as well as in my own surgical skills.

This patient had an uneventful surgical and postsurgical course, with a good visual outcome of 20/15 without haze, which is a typical outcome. The table shows my first 10 consecutive patients of 2013 who underwent bilateral PRK in my practice. By postoperative month 1, the mean visual acuity was 20/16 OU. By postoperative month 6, mean visual acuity was 20/15. In my experience, I feel Lotemax Gel controls pain well following ocular surgery. Careful screening and conservative patient selection most certainly play an important role in my outcomes.

PRK is highly effective, and long-term visual outcomes are comparable to LASIK.[5] It is easier, quicker, and cheaper to perform than LASIK, and potential flap complications are eliminated entirely. My patients experience good visual outcomes similar to that commonly seen with LASIK. For all of these reasons, I favor advanced surface ablation for laser vision correction surgery. ■

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INDICATION

LOTEMAX® GEL (loteprednol etabonate ophthalmic gel) 0.5% is indicated for the treatment of post-operative inflammation and pain following ocular surgery.

IMPORTANT SAFETY INFORMATION ABOUT LOTEMAX® GEL

- LOTEMAX® GEL 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.
- 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.
- Use of corticosteroids may result in posterior subcapsular cataract formation.
- Use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation and occurrence of perforations in those with diseases causing corneal and scleral thinning. 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, and, where appropriate, fluorescein staining.
- 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.
- Use 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 exacerbate the severity of many viral infections of the eye (including herpes simplex).
- 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.
- Patients should not wear contact lenses when using LOTEMAX® GEL.
- The most common ocular adverse drug reactions reported were anterior chamber inflammation (5%), eye pain (2%) and foreign body sensation (2%).

BAUSCH+LOMB

LOTEMAX®

loteprednol etabonate
ophthalmic gel 0.5%

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

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

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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.

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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 LOTEMAX.

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.

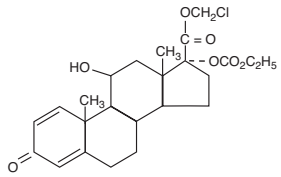
8.5 Geriatric Use

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

$C_{24}H_{31}ClO_7$ Mol. Wt. 466.96

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/glucocorticoid 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

Reference ID: 3196435
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