Combining strategies in the counseling and care of patients with cataracts
Introduction

More than three million cataract surgeries are performed in the United States each year,¹ and that number is expected to increase. The main objective for patients undergoing cataract surgery is to improve quality of vision. Cataract surgery causes inflammation; therefore, treatment of inflammation is important to the patient.

OCULAR SURGERY NEWS, with the support of Bausch + Lomb, gathered a panel of leading ophthalmologists during Hawaiian Eye 2016 to discuss treating postoperative ocular pain and inflammation following ocular surgery using LOTEMAX® Gel (loteprednol etabonate ophthalmic gel) 0.5% (Bausch + Lomb) and treating postoperative pain and inflammation following cataract surgery using PROLENSA® (bromfenac ophthalmic solution) 0.07% (Bausch + Lomb). The panel also discussed methods and tips for counseling patients on obtaining and administering these medications.

I thank the expert panelists for their participation, as well as Bausch + Lomb for sponsoring this OCULAR SURGERY NEWS supplement. For more educational materials on this topic, visit Healio.com/Ophthalmology/Education-Lab.

Richard L. Lindstrom, MD
Chief Medical Editor
OCULAR SURGERY NEWS

TABLE OF CONTENTS

A good corticosteroid choice for the routine ocular surgery patient .................... 3
Jodi I. Luchs, MD

An NSAID for powerful penetration of the cornea with once-daily dosing.......... 6
Karl G. Stonecipher, MD

The role of patient counseling .......... 10
Elizabeth Yeu, MD

INDICATIONS

Lotemax® Gel (loteprednol etabonate ophthalmic gel) 0.5% is a corticosteroid indicated for the treatment of postoperative inflammation and pain following ocular surgery.

Prolensa® (bromfenac ophthalmic solution) 0.07% is a nonsteroidal anti-inflammatory drug (NSAID) indicated for the treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery.

See Important Safety Information throughout, and full Prescribing Information for Prolensa and Lotemax Gel on pages 13-15.


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A good corticosteroid choice for the routine ocular surgery patient
Jodi I. Luchs, MD

Lotemax® Gel (loteprednol etabonate ophthalmic gel) 0.5% (Bausch + Lomb) is indicated for the treatment of postoperative inflammation and pain following ocular surgery. The gel is an ester-based corticosteroid with potent anti-inflammatory activity; it contains an ester group at the carbon-20 (C-20) position in place of a ketone group in the C-20 position.1,2 With this design, the drug is converted into inactive metabolites by esterases in the eye after it exerts its clinical effects.3 The dosing for Lotemax Gel is one to two drops into the conjunctival sac of the affected eye four times daily, starting the day after surgery and for 2 weeks postoperatively.

The formulation consists of many advancements that improve the delivery of the drug vs. the previous suspension formula. The first of these features is its mucoadhesive technology, which comes by virtue of the polycarbophil, a high molecular weight polymer, in the formulation.2 The gel is engineered to adhere to the ocular surface, remaining there for an extended period of time;4 however, it is not absorbed into the ocular tissue.5 The electrolytes in the tear film slowly release the loteprednol molecule from the matrix.

Another advanced feature is the adaptive viscosity technology. When this formulation is delivered from the bottle, it has the viscosity of a gel. Upon instillation into the eye and when subsequently combined with the stress from blinking and the electrolytes of the tear film, however, the viscosity decreases to close to the level of the viscosity of Lotemax suspension.2 This is relevant because the viscosity of Lotemax Gel allows the medication to adhere to the ocular surface.2

The non-settling formulation allows for uniform dosing. The gel formulation allows the loteprednol molecule to remain uniformly suspended without the need to shake the bottle, which is important because every drop coming out of the bottle has the same concentration of the drug that is labeled on the product. Also, as a result of this non-settling formulation, patients do not need to shake the bottle to re-suspend the drug before applying the drops. Therefore, physicians know that the patient will get the intended amount of medication from the beginning to the end of treatment.

The design of Lotemax Gel contains two moisturizers, glycerin and propylene glycol.2 In addition, Lotemax Gel has lower preservative concentration compared with...
Lotemax suspension.\(^2\) Finally, the pH has been changed to be centered at 6.5,\(^6\) which is close to the pH of natural tears.

Lotemax Gel has an established safety profile and is associated with decreased incidence of a rise in IOP when compared with prednisolone acetate.\(^1,7\) If a patient is being treated longer than 10 days with Lotemax Gel, then the patient’s IOP should be checked. Two phase 3 clinical trials designed as randomized, multicenter, double-masked, placebo controlled, parallel-group clinical trials were conducted. Patients who had significant inflammation (grade 2 or worse for anterior chamber cells 24 hours following surgery) after routine cataract surgery were enrolled in the trial. Each trial enrolled more than 400 patients. Patients self-administered one to two drops of either Lotemax Gel or the placebo four times a day for 14 days postoperatively.

The primary endpoint was complete resolution of the anterior chamber cells and complete resolution of pain at day 8. Researchers found that a significantly higher proportion of patients treated with Lotemax Gel had resolution of anterior chamber cells and complete resolution of pain when compared with the placebo (Figure, page 3).

In addition, the overall incidence of adverse events in the clinical trials was low. First, there were only two reported incidents of blurred vision, and these were within the vehicle group.\(^6,8\) Second, there were no statistically significant differences in the IOPs in the patients treated with Lotemax Gel compared with the placebo in either of the two clinical trials.\(^6,8\) The majority of patients reported no discharge, dryness, itching, pain, photophobia, or tearing in the group treated with Lotemax Gel. In fact, fewer patients in the Lotemax Gel group reported those symptoms compared with the placebo-treated group.\(^9\) These data can give physicians confidence in the drug’s ability to control inflammation in patients who are significantly inflamed after ocular surgery.

**Expert panel discussion**

**Richard L. Lindstrom, MD:** What has been your clinical experience with Lotemax Gel in terms of IOP?

**Jodi I. Luchs, MD:** For me, Lotemax Gel is a potent steroid. When the original Lotemax suspension was launched, physicians considered it a soft steroid because it did not raise IOP. My colleagues and I have started to use Lotemax Gel in patients following ocular surgery.

**Inder Paul Singh, MD:** As a glaucoma specialist, I perform a number of cataract surgeries on patients who have glaucoma. So far, using Lotemax Gel, my colleagues and I have not yet seen significant IOP spikes, however we are sure to monitor patients’ IOP if they are treated with the medication for more than 10 days. When treating patients with glaucoma, reducing the risk of increasing IOP is important; a high IOP spike in patients whose optic nerves are already significantly damaged can be problematic.

**Elizabeth Yeu, MD:** Lotemax Gel is an effective steroid for any intraocular or corneal surgery. Given its profile for lower IOP spikes, I preferentially use this potent steroid when performing cataract surgery in my patients who have glaucoma, as well as with my corneal and keratorefractive procedures.

**Mitchell A. Jackson, MD:** With any cataract or refractive cataract procedure, surgeons want to avoid IOP spikes, as this can exacerbate corneal edema and/or put any patient who has glaucoma at risk for further vision loss. I find that IOP rises are a minimal concern when using Lotemax Gel, given its safety and efficacy profile.

**Lindstrom:** In addition, one of the difficulties ophthalmologists face is the need to understand the chemistry of Lotemax Gel. Typically, ophthalmologists assume that with a potent steroid, pressure spikes are more likely. As a result, many specialists feel that if there is no pressure spike, then the steroid must not be potent. That can be true with the ketone steroids, but Lotemax Gel is an ester steroid. The potential for pressure spikes is not reduced because of lowered potency; the potential is reduced because the chemistry is different.

**Lindstrom:** What is Lotemax Gel’s effect on the ocular surface?

**IMPORTANT SAFETY INFORMATION (LOTMAX\(^\text{®}\) GEL)**

- 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.

- 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.

Please see Important Safety Information on pages 3-5 and Prescribing Information for LOTMAX\(^\text{®}\) Gel on pages 14-15.
William B. Trattler, MD: As Dr. Luchs noted in the introduction, Lotemax Gel contains two known moisturizers, glycerin and propylene glycol, and those ingredients bind water and moisture.

Lindstrom: It is worth noting that inflammation was reduced in as little as 8 days.

Singh: Lotemax Gel is the only ocular steroid formulation containing glycerin and propylene glycol, two known moisturizers, and has relatively low preservative concentration (0.003% benzalkonium chloride).

Lindstrom: Why is the non-settling formulation of Lotemax Gel important?

Karl G. Stonecipher, MD: According to one study, less than one-third of patients shake their topical ophthalmic medication prior to instillation. The non-settling formulation of Lotemax Gel eliminates the need to shake the bottle. With suspensions that require shaking, patients may not get the intended concentration of the drug if they do not shake the bottle. This does not happen with Lotemax Gel as Lotemax Gel has no requirement for shaking.

Luchs: Suspension formulations must be shaken to resuspend the medication before every dose. If the bottle is not shaken, then the patient may not get the intended concentration of the drug.

Jackson: I have my patients track the drops as they take them on a postoperative sheet with fill-in circles, so that they can accurately track their doses.

Lindstrom: Why is Lotemax Gel’s mucoadhesive technology important to its performance?

Yeau: The mucoadhesive technology of Lotemax Gel is formulated to provide sufficient contact time with the cornea, leading to intraocular penetration.

Luchs: This technology is important because the conjunctiva, one of the mucin-secreting surfaces to which it adheres, extends all the way to the palpebral conjunctiva, so there is a large surface area and plenty of room for penetration into the eye. Overall, this formulation represents an innovative step forward in topical corticosteroid technology.

References

4. LOTEMAX® GEL (loteprednol etabonate ophthalmic gel) 0.5% prescribing information. Bausch & Lomb Incorporated; Tampa, Fla. September 2012.

DOSAGE AND ADMINISTRATION: RECOMMENDED DOSING (LOTEMAX® GEL)

- Invert closed bottle and shake once to fill tip before instilling drops. Apply one to two drops of LOTEMAX® Gel 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.

IMPORTANT SAFETY INFORMATION (LOTEMAX® GEL)

- 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 infections.
- Use of a corticosteroid medication in 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).
- 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.
- Patients should not wear contact lenses when using LOTEMAX® Gel.
- The most common adverse drug reactions were anterior chamber inflammation (5%), eye pain (2%), and foreign body sensation (2%).

Please see Important Safety Information on pages 3-5 and Prescribing Information for LOTEMAX® Gel on pages 14-15.
An NSAID for powerful penetration of the cornea with once-daily dosing
Karl G. Stonecipher, MD

Prolensa® (bromfenac ophthalmic solution) 0.07% (Bausch + Lomb) is an NSAID indicated for the treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery. As mentioned earlier, cataract surgery is an increasingly common surgery in the United States. Postoperative pain and inflammation come about in many ways, but the key in all of the cases of pain and inflammation is getting the medication in the eye so that a response can be seen. The dosing for Prolensa is one drop into the affected eye(s) 1 day before surgery, one drop on the day of surgery, and one drop daily for 14 days following surgery. Prolensa is available in a 3-mL bottle size. Even if patients have difficulty with drop instillation, the 3-mL bottle provides enough medication to cover the treatment course.

Prostaglandins play a critical role in the generation of the inflammatory response, and this medication attempts to reduce prostaglandin levels. Prolensa is halogenated with bromine,1 and this chemical reaction increases the potency against cyclooxygenase-2 (COX-2),2 increases lipophilicity, and facilitates penetration through the cornea. Its lipophilicity helps to ensure penetration in the iris and ciliary body.

The formulation of Prolensa is designed for patient comfort and convenience. Patients reported less foreign body sensation and photophobia and had less redness versus the vehicle.3 Also, the formulation is buffered at a physiologic pH.4,5 The pH level of Prolensa is 7.8—close to that of natural tears, which is 7.5. Prolensa also has once-daily dosing.5

Another benefit of this medication is that the recommended dosing starts one day before surgery.5 Physicians find this beneficial for a few reasons. For example, in my practice, it is common for my patients not to fill the correct medication prescription and arrive for a presurgical office visit with medications other than what was prescribed. Requiring the medication to be used one day before surgery gives physicians the opportunity to ensure that the patient has the prescribed drug in their hands on the day of the actual surgery.

Prolensa has an established safety profile. Two double-masked, multicenter, placebo-controlled, randomized studies were conducted. Four hundred forty patients were included in these trials with 222 in the bromfenac group and 218 in the placebo group for a total of 440 study eyes.6 Dosing of the assigned medication began 1 day before surgery.5

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Figure 1. Percentage of summed ocular inflammation scores (SOIS) of grade 0 at study visit days 1, 3, 8 and 15.

Reprinted from Ophthalmology, 121/1, Walters TR, Goldberg DF, Peace JH, Gow JA; Bromfenac Ophthalmic Solution 0.07% Once Daily Study Group, Once Daily Study Group. Bromfenac ophthalmic solution 0.07% dosed once daily for cataract surgery: results of 2 randomized controlled trials, 25-33, Copyright (2014), with permission from Elsevier.

Figure 2. Percentage of subjects with ocular pain scores of grade 0 at study visit days 1, 3, 8 and 15.

Reprinted from Ophthalmology, 121/1, Walters TR, Goldberg DF, Peace JH, Gow JA; Bromfenac Ophthalmic Solution 0.07% Once Daily Study Group, Once Daily Study Group. Bromfenac ophthalmic solution 0.07% dosed once daily for cataract surgery: results of 2 randomized controlled trials, 25-33, Copyright (2014), with permission from Elsevier.

Please see Important Safety Information on pages 7-9 and Prescribing Information for PROLENSA® on page 13.
the day of surgery, and then continued for 14 days after surgery, for a total of 16 days of medication.5,6

Results of the clinical trials supported that Prolensa was effective at eliminating postoperative inflammation by day 15 (Figure 1), and a secondary efficacy outcome showed that a significant number of patients were pain free at each study visit (Figure 2).6,7 With regard to safety, occurrence of ocular and systemic adverse events was evaluated. Researchers found the rates of photophobia, foreign body sensation and redness were low when compared with the placebo, and the rate of discontinuation of the medication was also low.7

I have had the opportunity to prescribe Prolensa as a once-daily dosage since its approval. Most patients can obtain this medication through the majority of insurance plans, and even if patients are inaccurate with drop instillation, the bottle size provides the necessary amount of medication for a complete course of treatment. Prolensa can help control inflammation after surgery, which can occur in as little as 8 days.

**Expert panel discussion**

Richard L. Lindstrom, MD: What are your thoughts on the potency, efficacy, and safety profile of Prolensa?

Mitchell A. Jackson, MD: Halogenation is one of several ways for a molecule to have enhanced transmission into the eye through the hydrophobic corneal barrier, therefore the chemistry of the halogenated bromine molecule improves its potency. A lower pH is also advantageous as it is close to natural tears. The pH of Prolensa, along with the halogenated bromine molecule, crosses the hydrophobic cornea in a solution preparation that does not rely on a requirement to shake the bottle. In addition, pain, which was recorded on an ocular comfort diary, was less for Prolensa when compared with placebo.4

Jodi I. Luchs, MD: The collective mechanisms used to get this drug into the eye represent a beneficial approach. In particular, the lower pH of this 0.07% bromfenac formulation allows more of the drug to exist in the solution in its un-ionized state than other bromfenac formulations, which, in turn, allows more drug to penetrate into the eye where it can exert its potency.

Inder Paul Singh, MD: In addition to active ingredients and potency, the pH of Prolensa has positively impacted the absorption of the molecule.

Elizabeth Yeu, MD: I feel confident prescribing Prolensa for my patients undergoing cataract surgery. I have found it to be an effective, once-daily medication in reducing inflammation and pain in my patients undergoing cataract surgery.

William B. Trattler, MD: Prolensa has an excellent safety record. Patients have reported less foreign body sensation, less photophobia, and have had less redness versus the vehicle.3

Lindstrom: There are several factors that impact administration. For example, there is a low rate of blurred vision with Prolensa (Table, page 8). What do you like about Prolensa’s once-daily dosing protocol?

Luchs: For me, an aspect of the formulation is that the lower concentration of the drug compared to previous bromfenac formulations does not sacrifice anti-inflammatory efficacy.5,6

Lindstrom: What about Prolensa’s safety profile is most compelling?

Yeu: This formulation has good efficacy at once-daily dosing.

Singh: I also like the once-daily dosing regimen. Also, low rates of blurred vision have been reported with Prolensa (Table, page 8), and I also see that in my practice.

**INDICATIONS AND USAGE (PROLENSA®)**

- PROLENSA® (bromfenac ophthalmic solution) 0.07% is a nonsteroidal anti-inflammatory drug (NSAID) indicated for the treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery.

**IMPORTANT SAFETY INFORMATION (PROLENSA®)**

- The most commonly reported adverse reactions in 3% to 8% of patients were anterior chamber inflammation, foreign body sensation, eye pain, photophobia, and vision blurred.

- PROLENSA® contains sodium sulfite, a sulfite that may cause allergic type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

Please see Important Safety Information on pages 7-9 and Prescribing Information for PROLENSA® on page 13.
Trattler: Many of us perform femtosecond laser cataract surgeries on a regular basis, and with that, we write many prescriptions for anti-inflammatory medications. I like that my patients only have to instil one drop of Prolensa once a day for the indicated time.

Lindstrom: What is the benefit of prescribing Prolensa and Lotemax Gel for the treatment of patients undergoing laser cataract surgery?

Luchs: I prescribe Prolensa because it inhibits cyclooxygenase-2 (COX-2). I prescribe Lotemax Gel because it is indicated to treat inflammation and pain following ocular surgery. Lotemax Gel and Prolensa work at different points in the inflammatory pathways responsible for the production of prostaglandins, which in turn, can cause postoperative inflammation.

Yeu: I have prescribed Prolensa and Lotemax Gel frequently for cataract surgery. In my glaucoma patients undergoing cataract surgery, I prescribe Lotemax Gel because of the efficacy it provides and its limited impact on IOP. I always check my patients’ IOP levels if they are being treated longer than 10 days on this medication. I prescribe Prolensa because it gives efficacy with once-daily dosing.

Jackson: I am up to performing 92% of cases with a femtosecond laser, and so my routine is to prescribe Lotemax Gel four times a day. In certain patients, I will prescribe Prolensa once daily following cataract surgery. As we know, Lotemax Gel and Prolensa independently address inflammation postoperatively at different points in the arachidonic acid pathway.

Singh: I perform approximately 50% of my cataract surgery with the femtosecond laser. Most of these patients have arcuate incisions, and therefore, I want to decrease inflammation and decrease pain postoperatively. In my experience, Prolensa, which is prescribed

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**Table. Prolensa safety profile**

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<tr>
<th></th>
<th>Eastern Region</th>
<th>Western Region</th>
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<tbody>
<tr>
<td><strong>Prolensa (n=109)</strong></td>
<td><strong>Placebo (n=102)</strong></td>
<td><strong>Prolensa (n=103)</strong></td>
</tr>
<tr>
<td>No. of patients with ≥1 ocular AE*</td>
<td>18 (16.5%)</td>
<td>24 (23.5%)</td>
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<tr>
<td>Anterior chamber inflammation</td>
<td>1.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Foreign body sensation</td>
<td>2.8%</td>
<td>4.9%</td>
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<tr>
<td>Eye pain</td>
<td>2.8%</td>
<td>5.9%</td>
</tr>
<tr>
<td>Vision blurred</td>
<td>0.0%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Increased IOP</td>
<td>0.9%</td>
<td>1.0%</td>
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</table>


*adverse events

Summary of Prolensa’s safety profile. This table contains some of the possible safety considerations and their reported occurrence.

Please see Important Safety Information for Prolensa on pages 7-9.

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**DOSEAGE AND ADMINISTRATION: RECOMMENDED DOSING (PROLENSA®)**

- One drop of PROLENSA® ophthalmic solution should be applied to the affected eye once daily beginning 1 day prior to cataract surgery, continued on the day of surgery, and through the first 14 days of the postoperative period.

**IMPORTANT SAFETY INFORMATION (PROLENSA®)**

- The most commonly reported adverse reactions in 3%-8% of patients were anterior chamber inflammation, foreign body sensation, eye pain, photophobia, and blurred vision.

Please see Important Safety Information on pages 7-9 and Prescribing Information for PROLENSA® on page 13.
for pain and inflammation in patients who have undergone cataract surgery, has done a good job in achieving these goals for patients.

References

IMPORTANT SAFETY INFORMATION (PROLENSA®)
- PROLENSA® contains sodium sulfite, a sulfite that may cause allergic type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.
- All topical nonsteroidal anti-inflammatory drugs (NSAIDs), including bromfenac, may slow or delay healing. Topical corticosteroids are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.
- There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs, including bromfenac. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.
- There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery. Use with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.
- Use of topical NSAIDs may result in keratitis. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of topical NSAIDs, including bromfenac, and should be closely monitored for corneal health. Patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases (e.g., dry eye syndrome), rheumatoid arthritis, or repeat ocular surgeries within a short period of time may be at increased risk for corneal adverse events which may become sight threatening. Topical NSAIDs should be used with caution in these patients. Post-marketing experience with topical NSAIDs suggests that use more than 24 hours prior to surgery or use beyond 14 days post-surgery may increase patient risk for the occurrence and severity of corneal adverse events.
- PROLENSA® should not be instilled while wearing contact lenses. Remove contact lenses prior to instillation of PROLENSA®. The preservative in PROLENSA®, benzalkonium chloride may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of PROLENSA®.

Please see Prescribing Information for PROLENSA® on page 13.
The role of patient counseling
Elizabeth Yeu, MD

To have good surgical outcomes, it is important to plan and address postoperative care and counseling even before the surgery. With strong preoperative care, physicians can reduce the amount of time spent with a patient postoperatively, and this is important for surgeons with a high volume of patients to be efficient.

To ensure the postoperative period goes smoothly, I have a specific conversation with each of my patients. I start by explaining that we will take a well-rounded approach using all of the extensive diagnostic information collected preoperatively. I am careful to demonstrate my appreciation for the patient’s time, which can sometimes be up to 3 or 4 hours of testing and examinations from start to finish. I explain that upon completion of the surgery, it is important for the eye to heal correctly for the patient to be satisfied with the results. My staff and I do everything on our end toward this outcome, but once the patient leaves the operating room, the responsibility of daily care falls to him or her to heal well.

As a result, a significant portion of this conversation is counseling patients on how to ensure they receive the specific medications I prescribe. Throughout my counseling process, particularly with my patients who have glaucoma and are undergoing cataract surgery, I explain that I prescribe both Prolensa® (bromfenac ophthalmic solution) 0.07% (Bausch + Lomb) and Lotemax® Gel (loteprednol etabonate ophthalmic gel) 0.5% (Bausch + Lomb) because I believe their effects are worth the cost. I mention the availability of copay assistance coupons that can help assist with the cost. I inform patients that there is no approved, generic equivalent of either Lotemax Gel or Prolensa, and there are numerous reasons for my prescribing these specific medications. Both medications have established safety profiles. For example, with Prolensa, clinical trial results showed that less than 3% to 8% of the treated population had complaints of discomfort or vision issues.

It is important to state clearly and with conviction that the prescribed medications are the ones patients should obtain. That is why explaining the features and the reasons to every patient is critical. I make sure to have a stack of copay assistance coupons accessible for distribution. Finally, it is important that the patient understands that some pharmacists may offer them alternative choices, and that they may have to be firm with the pharmacist to fill the prescription as prescribed. I provide my patients with the rationale to ask for the medications as prescribed to ensure their postoperative care. This can make a difference for the patient’s willingness to fill the recommended prescription.

Expert panel discussion
Richard L. Lindstrom, MD: Is proper administration of the drops part of counseling patients? If so, what are the provided instructions?

Inder Paul Singh, MD: We instruct patients to administer any drops 5 minutes apart. In general, based on the product information for most of the ocular medications we use, 95% or more of the drug is absorbed within 5 minutes, which is why I have my patients wait at least 5 minutes between any drops to avoid washing the first drop away or “diluting” the drop. Our instruction sheet contains small circles for patients to fill in when they take their drops so they can remember when they administered them. The number of circles on the sheet indicates the number of drops that should be administered, and this aids the patient in tracking their medications. Also, when I see the patient on the day after surgery, I will put the first set of drops in as I am talking to the patient.

Mitchell A. Jackson, MD: With the indicated dosing protocol, I also teach patients to space any drops 5 minutes apart. Most topical eye medications lose their effective volume through the nasolacrimal pathway once administered. It is important for patients to wait at least 3 to 5 minutes to avoid an additional unnecessary dilution effect, which could impact the drops full therapeutic effect.

Elizabeth Yeu, MD: Lotemax Gel has the mucoadhesive technology, and both

DOSAGE AND ADMINISTRATION: RECOMMENDED DOSING (LOTEMAX®)
- 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 postoperative period.

DOSAGE AND ADMINISTRATION: RECOMMENDED DOSING (PROLENSA®)
- One drop of PROLENSA® ophthalmic solution should be applied to the affected eye once daily beginning 1 day prior to cataract surgery, continued on the day of surgery, and through the first 14 days of the postoperative period.

Please see Important Safety Information throughout, and Prescribing Information for LOTEMAX Gel® and PROLENSA® on pages 13-15.
Prolensa and Lotemax Gel have dose uniformity, and it is reassuring to know the Lotemax Gel formulation will help the medicine to adhere.

Lindstrom: In my practice, we have multiple conversations with patients about using the branded medications I prescribe, but issues still sometimes arise. For example, in Minnesota I can write “dispense as written,” or “do not substitute,” yet the pharmacist still can substitute with a generic medication, even without asking the patient. What strategies do you employ to ensure the pharmacist fills the prescription as it is written?

Jackson: I emphasize that, although the majority of the work is the surgery itself, the postoperative process falls to patients because they are the ones who have to administer the drops. In Illinois, pharmacists cannot automatically substitute medications, so it is an advantage for me. I make patients commit to their own outcome, and I explain to my patients the importance of the prescribed eye drops because of the nature of this one-time surgery.

Our process is to include wording such as “Dispense as written” or “Do not substitute” with a medical description included on every prescription. So now, most of my local pharmacists know to just fill the prescription as written. However, if they do call for prior authorization, my technicians are informed as to what to do. If a patient still insists on a generic, they must come to the office and sign a waiver form as another layer of protection for me because there is no generic equivalent. Sometimes, this extra step deters patients from further requesting a generic with a different concentration, and they then get the medications I prescribe.

Singh: I think the key for success in keeping my patients on the prescribed regimen is threefold: being clear about the need for the specifically prescribed products, educating patients and unifying a knowledgeable staff. First, physicians must convey to the patient the quality and need for the selected products. It is important to give patients enough understanding what has been prescribed and what the pharmacists may try to suggest.

If a patient goes to the pharmacy and the pharmacist mentions a less expensive product, the patient may be interested. However, it is through patient counseling that physicians educate the patient that it is not just about the cost—it is about the consistency, effectiveness and safety of the medication. I also tell patients there is no generic equivalent to the formulations of Prolensa or Lotemax Gel.

Second, my practice is aggressive in our method to educate patients. We are clear that we prefer the prescribed medication. They are also made aware that they may be offered a substitution at the pharmacy that is said to be the “same thing.” Our goal is to ensure patients are

“I tell patients there is no generic equivalent to the formulations of Prolensa and Lotemax Gel.” — INDER PAUL SINGH, MD

INDICATIONS AND IMPORTANT SAFETY INFORMATION (LOTEMAX®)

- LOTEMAX® Gel (loteprednol etabonate ophthalmic gel) 0.5% is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.
- 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.
- 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, intraocular pressure should be monitored.

INDICATIONS AND IMPORTANT SAFETY INFORMATION (PROLENSA®)

- PROLENSA® (bromfenac ophthalmic solution) 0.07% is a nonsteroidal anti-inflammatory drug (NSAID) indicated for the treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery.
- PROLENSA® contains sodium sulfite, a sulfite that may cause allergic type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.
- All topical nonsteroidal anti-inflammatory drugs (NSAIDs), including bromfenac, may slow or delay healing. Topical corticosteroids are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.

Please see Important Safety Information throughout, and Prescribing Information for LOTEMAX® Gel and PROLENSA® on pages 13-15.
prepared for this offer, and to educate them that it is not, in fact, exactly the same thing as the prescribed medication. The patient can then reiterate to the pharmacist that they want the prescription filled as written. This empowers patients to take it into their hands and to be knowledgeable about their medications.

Finally, it is important to make sure staff members are knowledgeable of the products and of this process. The staff members are key in reducing callbacks, especially if they are knowledgeable of the products and the reasons for prescribing them—meanwhile reiterating the patient’s request, too. Knowledgeable staff members are more likely to take the time to call the pharmacy back, and request the pharmacist keep patients on the originally prescribed medications.

William B. Trattler, MD: Typically, we give all our patients copay assistance coupons when available, and my technicians ensure the patients are educated on the branded medications I prefer, emphasizing there is no generic equivalent to Prolensa or Lotemax Gel. The technicians work hard to have the patients obtain the prescribed drops before undergoing surgery.

Stonecipher: I inform patients that, when appropriate, I will prescribe generic formulations, but when it comes to certain surgeries, I choose what I believe is the appropriate medication. I explain the need for these specific medications, and then I actively work with patients so they understand that we are trying to help them get their medications at the best price. For example, we suggest using pharmacies that we have researched and where prescription copay assistance coupons for those particular medications are best used. If they are from outside the local area, we have patients download the application on their phone and help them search for the pricing and copay assistance coupons that are best found in their area.

Lindstrom: Which features of Prolensa and Lotemax Gel do you highlight for patients?

Luchs: I highlight the efficacy and safety of both of these products. There are no generics currently available for these drugs.

Singh: I think dose uniformity and the addition of known moisturizers to the vehicle are the two main points I bring up with patients regarding Lotemax Gel. I do not have to worry about patients shaking the bottle, and I am comfortable with the low-level of preservative. For Prolensa, I tell patients it is a low concentration of active medication that has an established safety profile, and Prolensa once-daily dosing is an important feature.

Jackson: I explain to my patients that both Prolensa and Lotemax Gel have been through proven clinical trials that support their efficacy.

Lindstrom: I think physicians will see significant growth in the use of these drugs because of the proven efficacy and established safety profiles. As we close this discussion, I would like to thank the expert panel for their time and input, as well as Bausch + Lomb for its sponsorship of this supplement.

REFERENCES
4. Flach AJ. The importance of eyelid closure and nasolacrimal occlusion following the ocular instillation of topical glaucoma medications, and the need for the universal inclusion of one of these techniques in all patient treatments and clinical studies. Trans Am Ophthamol Soc. 2008; 106:138-48.

IMPORTANT SAFETY INFORMATION (LOTEMAX®)

- 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.

IMPORTANT SAFETY INFORMATION (PROLENSA®)

- There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs, including bromfenac. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

Please see Important Safety Information throughout, and Prescribing Information for LOTEMAX® Gel and PROLENSA® on pages 13-15.
3 DOSAGE FORMS AND STRENGTHS

Topical ophthalmic solution: bromfenac 0.07% (3)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Use of PROLENSA during pregnancy has not been studied. It is known that nonsteroidal anti-inflammatory drugs (NSAIDs) can cause fetal abnormalities when administered to pregnant rats at doses that are comparable to the human systemic exposure.

8.4 Pediatric Use

Safety and efficacy in pediatric patients below the age of 18 years have not been established.

8.5 Nursing Mothers

It is not known whether bromfenac is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when PROLENSA is administered to a nursing woman.

9 DESCRIPTION

Bromfenac sodium is a yellow to orange crystalline powder. Bromfenac sodium is designated chemically as sodium (2-aminophenyl)acetic acid, with the structural formula for bromfenac sodium as (H2N\textsubscript{2}O\textsubscript{4})\textsubscript{2}Na\textsubscript{2}\textsubscript{2}O\textsubscript{2}.

10 CLINICAL STUDIES

10.1 Mechanism of Action

Bromfenac is a non-steroidal anti-inflammatory drug (NSAID) that inhibits prostaglandin synthesis by inhibiting cyclooxygenase (COX) 1 and 2. Bromfenac has been shown in many animal models to be mediators of certain kinds of intraocular inflammation. In studies performed in animal eyes, proteoglycans have been shown to produce disruption of the blood-aqueous humor barrier, vasodilation, increased vascular permeability, leukocytosis, and increased intraocular pressure.

10.2 Pharmacokinetics

In humans, the plasma concentration of bromfenac following ophthalmic administration is 0.07% of the recommended human ophthalmic dose (HOD) assuming the human systemic concentration is at the limit of quantification and the ratio at oral doses up to 7.5 mg/kg/day (equivalent to 0.07% in the predicted human systemic exposure) produced no treatment-related alterations in reproduction studies. However, embryotoxic-fetal toxicity was not determined in rats and rabbits at 0.09 mg/kg/day and 7.5 mg/kg/day, respectively. In rat, bromfenac treatment caused delayed parturition at 0.03 mg/kg/day (30 times the predicted human exposure), and caused dystocia, increased neonatal mortality and reduced postnatal growth at 0.9 mg/kg/day (90 times the predicted human exposure).

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Because of the known effects of prostaglandin biosynthesis-inhibiting drugs on the fetal cardiovascular system (closure of ductus arteriosus), the use of PROLENSA ophthalmic solution during pregnancy should be avoided.

8.3 Nursing Mothers

Caution should be exercised when PROLENSA ophthalmic solution is administered to a nursing woman.

8.5 Pediatric Use

Safety and efficacy in pediatric patients below the age of 18 years have not been established.

8.6 Geriatric Use

There is evidence in non-steroidal anti-inflammatory drugs (NSAIDs) of increased risk of cardiovascular adverse events in patients aged 70 years of age and older compared to younger adult patients.

11 DESCRIPTION

11.2 Mechanism of Action

Bromfenac is a non-steroidal anti-inflammatory drug (NSAID) that inhibits prostaglandin synthesis by inhibition of cyclooxygenase (COX) 1 and 2. Bromfenac is a non-steroidal anti-inflammatory drug (NSAID) that inhibits prostaglandin synthesis by inhibition of cyclooxygenase (COX) 1 and 2. Bromfenac has been shown in many animal models to be mediators of certain kinds of intraocular inflammation. In studies performed in animal eyes, proteoglycans have been shown to produce disruption of the blood-aqueous humor barrier, vasodilation, increased vascular permeability, leukocytosis, and increased intraocular pressure.

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The plasma concentration of bromfenac following ophthalmic administration is 0.07% of the recommended human ophthalmic dose (HOD) assuming the human systemic concentration is at the limit of quantification and the ratio at oral doses up to 7.5 mg/kg/day (equivalent to 0.07% in the predicted human systemic exposure) produced no treatment-related alterations in reproduction studies. However, embryotoxic-fetal toxicity was not determined in rats and rabbits at 0.09 mg/kg/day and 7.5 mg/kg/day, respectively. In rat, bromfenac treatment caused delayed parturition at 0.03 mg/kg/day (30 times the predicted human exposure), and caused dystocia, increased neonatal mortality and reduced postnatal growth at 0.9 mg/kg/day (90 times the predicted human exposure).

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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 postoperative 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, 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

Revised: 08/2016
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 coincidently 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
Loteprednol etabonate has been shown to be embryotoxic (delayed ossification) and teratogenic (increased incidence of meningocoele, 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 Structure of Loteprednol Etabonate](http://example.com/loteprednol-structure.png)

Chemical Name:
chloromethyl 17α-[ethoxyxarbyloxy]-11β-hydroxy-3-oxoandrosta-1, 4-diene-17β-carboxylate

Each gram contains:
ACTIVE: Loteprednol Etabonate 5 mg (0.5%);
INACTIVES: Boric acid, edetate disodium dihydrate, glycerin, polycarbophil, propylene glycol, sodium chloride, tyoxefol, 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, fibrinolysis, 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 oculair 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 15º-25º C (59º-77º 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.