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ANNUAL CATARACT SURGERY ISSUE

Refining Postop Infection Prevention

Combining drops in one bottle and the use of postop injections are just part of the discussion. P. 26

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• First Look at Cutting-edge Retinal Therapies P. 58
Indications and Usage
BromSite® (bromfenac ophthalmic solution) 0.075% is a nonsteroidal anti-inflammatory drug (NSAID) indicated for the treatment of postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery.

Recommended Dosing
One drop of BromSite® should be applied to the affected eye twice daily (morning and evening) 1 day prior to surgery, the day of surgery, and 14 days postsurgery.

Important Safety Information
• Slow or Delayed Healing: All topical nonsteroidal anti-inflammatory drugs (NSAIDs), including BromSite®, 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.
• Potential for Cross-Sensitivity: There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs, including BromSite®. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.
• Increased Bleeding Time of Ocular Tissue: With some NSAIDs, including BromSite®, there exists the potential for increased bleeding time due to interference with platelet aggregation. There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery. It is recommended that BromSite® be used with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.
• Keratitis and Corneal Effects: Use of topical NSAIDs may result in keratitis. In some susceptible patients, continued use of topical NSAIDs may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or corneal perforation. Patients with evidence
The **FIRST** and **ONLY** NSAID indicated to prevent ocular pain in cataract surgery patients\(^1\)

**A DROP OF PREVENTION**

FOR YOUR CATARACT SURGERY PATIENTS

Defend against ocular pain and combat postoperative inflammation with the penetrating power of BromSite\(^\text{®}\) formulated with DuraSite\(^\text{®}\)

- DuraSite\(^\text{®}\) increases ocular surface retention time, resulting in increased bromfenac absorption\(^2\text{-}^5\)
- Provides 24-hour coverage with BID dosing\(^1\)
- Available in 5 mL bottle

Visit bromsite.com to find out more.

**Adverse Reactions:** The most commonly reported adverse reactions in 1% to 8% of patients were anterior chamber inflammation, headache, vitreous floaters, iritis, eye pain, and ocular hypertension.

Please see brief summary of Full Prescribing Information on the adjacent page.

NSAID=nonsteroidal anti-inflammatory drug.

References:
2. Hosseini K, Hutcheson J, Bowman L. Aqueous humor concentration of bromfenac 0.09% (Bromday\(^\text{™}\)) compared with bromfenac in DuraSite 0.075% (BromSite\(^\text{™}\)) in cataract patients undergoing phacoemulsification after 3 days dosing. Poster presented at: ARVO Annual Meeting; May 5-9, 2013; Seattle, Washington, 3. ClinicalTrials.gov. Aqueous humor concentration of InSite Vision (ISV) 303 (bromfenac in DuraSite) to Bromday once daily (QD) prior to cataract surgery. https://clinicaltrials.gov/ct2/show/results/NCT01387464?sect=X07156&term=insite+vision&rank=1. Accessed March 2, 2017.

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SUN-OPH-BRO-219 03/2017
BromSite® (bromfenac ophthalmic solution) 0.075%

INDICATIONS AND USAGE
BromSite® (bromfenac ophthalmic solution) 0.075% is indicated for the treatment of postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery.

CONTRAINDICATIONS
None

WARNINGS AND PRECAUTIONS
Slow or Delayed Healing
All topical nonsteroidal anti-inflammatory drugs (NSAIDs), including BromSite® (bromfenac ophthalmic solution) 0.075%, 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.

Potential for Cross-Sensitivity
There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs, including BromSite® (bromfenac ophthalmic solution) 0.075%. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

Increased Bleeding Time of Ocular Tissue
With some NSAIDs, including BromSite® (bromfenac ophthalmic solution) 0.075%, there exists the potential for increased bleeding time due to interference with platelet aggregation. There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery.

It is recommended that BromSite® be used with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.

Keratitis and Corneal Reactions
Use of topical NSAIDs may result in keratitis. In some susceptible patients, continued use of topical NSAIDs may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or corneal perforation. These events may be sight threatening. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of topical NSAIDs, including BromSite® (bromfenac ophthalmic solution) 0.075%, and should be closely monitored for corneal health.

Post-marketing experience with topical NSAIDs suggests that 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 also suggests that use more than 24 hours prior to surgery or use beyond 14 days postsurgery may increase patient risk for the occurrence and severity of corneal adverse events.

Contact Lens Wear
BromSite® should not be administered while wearing contact lenses. The preservative in BromSite®, benzalkonium chloride, may be absorbed by soft contact lenses.

ADVERSE REACTIONS
The following serious adverse reactions are described elsewhere in the Brief Summary:
- Slow or Delayed Healing
- Potential for Cross-Sensitivity
- Increased Bleeding Time of Ocular Tissue
- Keratitis and Corneal Reactions
- Contact Lens Wear

Clinical Trial Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The most commonly reported adverse reactions in 1–8% of patients were: anterior chamber inflammation, headache, vitreous floaters, iritis, eye pain and ocular hypertension.

USE IN SPECIFIC POPULATIONS
Pregnancy
Risk Summary
There are no adequate and well-controlled studies in pregnant women to inform any drug associated risks. Treatment of pregnant rats and rabbits with oral bromfenac did not produce teratogenic effects at clinically relevant doses.

Clinical Considerations
Because of the known effects of prostaglandin biosynthesis-inhibiting drugs on the fetal cardiovascular system (closure of ductus arteriosus), the use of BromSite® during late pregnancy should be avoided.

Data
Animal Data
Treatment of rats with bromfenac at oral doses up to 0.9 mg/kg/day (195 times a unilateral human ophthalmic dose on a mg/m² basis, assuming 100% absorbed) and rabbits at oral doses up to 7.5 mg/kg/day (3243 times a unilateral daily dose on a mg/m² basis) produced no structural teratogenicity in reproduction studies. However, embryo-fetal lethality, neonatal mortality and reduced postnatal growth were produced in rats at 0.9 mg/kg/day, and embryo-fetal lethality was produced in rabbits at 7.5 mg/kg/day. 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.

Lactation
There are no data on the presence of bromfenac in human milk, the effects on the breastfed infant, or the effects on milk production; however, systemic exposure to bromfenac from ocular administration is low. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for bromfenac and any potential adverse effects on the breast-fed child from bromfenac or from the underlying maternal condition.

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

Geriatric Use
There is no evidence that the efficacy or safety profiles for BromSite® differ in patients 65 years of age and older compared to younger adult patients.

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis and Impairment of Fertility
Long-term carcinogenicity studies in rats and mice given oral doses of bromfenac up to 0.6 mg/kg/day (129 times a unilateral daily dose assuming 100% absorbed, on a mg/m² basis) and 5 mg/kg/day (540 times a unilateral daily dose on a mg/m² basis) respectively revealed no significant increases in tumor incidence. Bromfenac did not show mutagenic potential in various mutagenicity studies, including the bacterial reverse mutation, chromosomal aberration, and micronucleus tests.

Bromfenac did not impair fertility when administered orally to male and female rats at doses up to 0.9 mg/kg/day and 0.3 mg/kg/day, respectively (195 and 65 times a unilateral daily dose, respectively, on a mg/m² basis).

Rx Only
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SUN-OPH-BRO-017-1 03/2017
The Prescription Drug Price Relief Act of 2019 was recently introduced to lawmakers, aiming to allow generic drug companies to enter into competition with patent-holding drug manufacturers after a petitioned drug’s price is deemed excessive. With hearings on drug prices under way, all constituents are being heard, from doctors and patients to members of the pharmaceutical industry.

The bill would allow the Secretary of Health and Human Services to deem a petitioned drug excessively priced if its U.S. price is higher than that of its median price in the United Kingdom, Canada, Germany, France and Japan. However, if that stipulation is not met, the Secretary can still judge the price excessively high by taking into account factors such as the following:

- size of the affected patient population;
- value of the drug to patients;
- costs associated with development of the drug;
- whether the drug produces a significant improvement in health outcomes; and
- cumulative global revenues generated by the drug.

Once confirmed to be excessively high, the pharmaceutical company would have to lower the drug’s price. Otherwise, the government would allow a generic manufacturer to enter production by waiving or voiding any government-granted exclusivities. However, the generic manufacturer would pay a reasonable royalty to the company that holds the patent. This could be a percentage of sales or an amount that’s determined by the Secretary based on factors similar to those already listed.

According to Michael Repka, MD, the AAO Medical Director for Government Affairs, this kind of sweeping legislation doesn’t seem likely. While industry and doctors can somewhat agree that drug prices are too high, both parties highlight issues associated with the bill. “Setting our prices based upon what [drugs] cost in Europe or other parts of the world is an idea that doesn’t seem politically palatable to anyone,” Dr. Repka says. However, he acknowledges that relief is necessary. “As a physician-advocate for our patients, drug prices are high and many consumers can’t afford them.”

The Pharmaceutical Research and Manufacturers of America sees the bill as flawed. The organization says that patients won’t benefit from the legislation, and that it may affect America’s position as a pharmaceutical leader. “Circumventing patent and other intellectual property rights on medical innovation, and allowing foreign governments to set U.S. prices, would be disastrous for patients,” PhRMA said in a prepared statement. The organization is concerned that reduced investment in research and development may slow progress in creating tomorrow’s cures, and could result in Americans having access to fewer new medicines. PhRMA adds that there’s no evidence the bill would benefit patient access or affordability of the medicine. “Patients in countries whose governments set prices wait years for new medicines and have far fewer treatment options,” the organization’s statement added.

PhRMA also feels the bill could harm America’s competitive pharmaceutical status on the world stage. “No countries that are leaders in innovation have taken such drastic measures,” it remarked. “These policies would threaten America’s ability to remain competitive and instead, replicate flawed policies of countries where patient needs are brushed aside.”

Dr. Repka details several of the factors that will go into any legislation affecting drug prices. First, he notes that different nations bear different costs associated with pharma-
centicals. “Industry has research and development but they also have marketing and advertising and, in some countries, these costs may not exist at the same levels,” he says. “Choosing average overseas pricing as a vehicle to price medications in our own economy doesn’t seem consistent with a market-based economy.”

Feasibility of producing additional generic drugs is another potential issue. “Part of this bill seeks to move branded drugs to the generic space,” Dr. Repka says, “but we may not have the generic capacity to produce them. We have problems of shortages in the generic space, and ramping up production for a limited market can be very expensive.” He says that this could pose a risk to patients if medications aren’t sufficiently profitable. “We have to have a price that’s high enough that industry is willing to bring it to market, but also a price that the consumer can afford,” he adds.

When asked if patients who take medication for chronic conditions (i.e., patients with dry eye or glaucoma) may opt for medical treatment instead of surgical intervention if drug prices were to come down, Dr. Repka says it’s possible. “In general, pharmacotherapy is used before surgical therapy,” he notes, “but lower pricing could cause patients to be willing to continue long-term pharmacotherapy or a multidrug plan.”

On the question of whether drug prices are fair or if there’s an alternative solution, PhRMA notes that large rebates are often required for a medicine to be covered. “Forty percent of the list price of medicines is given as rebates or discounts to insurance companies, the government, Pharmacy Benefit Managers and other entities in the supply chain,” the organization says. PhRMA notes that these savings are often not shared with patients, whose out-of-pocket costs soar as rebates and discounts grow every year. “We need to ensure that more of the negotiated rebates and discounts are resulting in lower costs for patients at the pharmacy,” the industry group says. Dr. Repka acknowledges that rebates could be a subject to explore, noting, “They’re generally not transparent to the consumer.”

In terms of alternative solutions, Dr. Repka says improved transparency in drug-pricing reform is needed to protect patients. “Any drug-price legislation in the U.S. has to help the consumer understand where their payments go so that they buy the right plan,” he says. “Weakening patient protection or shortening the period it takes for generic companies to gain access to producing these medications is the only thing I could see happening. This bill does that, but with a very sharp knife. Changing the patent process or changing exclusivity terms seem to be very significant changes in how we go about protecting intellectual property. There would have to be enough protections for the manufacturer’s rights.”

Dr. Repka concludes, “I think that everyone recognizes that prices are too high. We need [both] pricing and availability—so it’s a very difficult needle to thread.”

At press time, hearings had just

(Continued on page 16)
Experiencing zero-energy lens fragmentation.

ZEISS miLOOP

Keep the zonules intact

The new miLOOP® from ZEISS is a micro-interventional device, developed to deliver zero-energy1 lens fragmentation and achieve full-thickness lens fragmentation. The dissecting action of ZEISS miLOOP is designed to reduce force on the delicate capsular bag and zonules.

Lens cracking

Lens fragmentation with ZEISS miLOOP

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INDICATIONS AND USAGE

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 ABOUT PROLENSA®

• PROLENSA® contains sodium sulftte, a sulftte 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 sulftte sensitivity in the general population is unknown and probably low. Sulftte 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. 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. Use with caution in patients 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. The preservative in PROLENSA®, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of 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 brief summary of full Prescribing Information for PROLENSA® on adjacent page.
Clinical Trial Experience

Drug interactions involving topical and ocular preparations of bromfenac are not expected. However, due to the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs, including bromfenac, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

Increased Bleeding Time

With some NSAIDs, including bromfenac, there exists the potential for increased bleeding time due to interference with platelet aggregation. There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems. Potential for Cross-Sensitivity

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.

Sterility of Dropper Tip

The dropper tip is single use and should not be used to administer more than one bottle of PROLENSA. The dropper tip is reinfused into the bottle when not in use.

Contact Lens Wear

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.

ADVERSE REACTIONS

Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. The most commonly reported adverse reactions following use of PROLENSA ophthalmic solution following cataract surgery include: anterior chamber inflammation, foreign body sensation, eye pain, photophobia and vision blurred. These reactions were reported in 3 to 8% of patients.

USE IN SPECIFIC POPULATIONS

Pregnancy

Treatment of rats at oral doses up to 0.9 mg/kg/day (systemic exposure 90 times the systemic exposure predicted from the recommended human ophthalmic dose [RHOD] assuming the human systemic concentration is at the limit of quantification) and rabbits at oral doses up to 7.5 mg/kg/day (150 times the predicted human systemic exposure) produced no treatment-related malformations in reproduction studies. However, embryo-fetal lethality and maternal toxicity were produced in rats and rabbits at 0.9 mg/kg/day and 7.5 mg/kg/day, respectively. In rats, bromfenac treatment caused delayed parturition at 0.3 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.

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 late pregnancy should be avoided.

Nursing Mothers

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

Pediatric Use

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

Geriatric Use

There is no evidence that the efficacy or safety profiles for PROLENSA differ in patients 70 years of age and older compared to younger adult patients.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis and Impairment of Fertility

Long-term carcinogenicity studies in rats and mice given oral doses of bromfenac up to 0.6 mg/kg/day (systemic exposure 50 times the systemic exposure predicted from the recommended human ophthalmic dose [RHOD] assuming the human systemic concentration is at the limit of quantification) and 5 mg/kg/day (340 times the predicted human systemic exposure), respectively, revealed no significant increases in tumor incidences. Bromfenac did not show mutagenic potential in various mutagenicity studies, including the reverse mutation, chromosomal aberration, and micronucleus tests. Bromfenac did not impair fertility when administered orally to male and female rats at doses up to 0.9 mg/kg/day and 0.3 mg/kg/day, respectively (systemic exposure 90 and 30 times the predicted human exposure, respectively).

PATIENT COUNSELING INFORMATION

Slowed or Delayed Healing

Advise patients of the possibility that slow or delayed healing may occur while using NSAIDs.

Sterility of Dropper Tip

Advise patients to replace bottle cap after using and to not touch dropper tip to any surface, as this may contaminate the contents. Advise patients that a single bottle of PROLENSA should be used to treat only one eye.

Concomitant Use of Contact Lenses

Advise patients to 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.

Concomitant Topical Ocular Therapy

If more than one topical ophthalmic medication is being used, the medicines should be administered at least 5 minutes apart.

PATIENT COUNSELING INFORMATION

SLOWED OR DELAYED HEALING

Advise patients of the possibility that slow or delayed healing may occur while using NSAIDs.

STERILITY OF DROPPER TIP

Advise patients to replace bottle cap after using and to not touch dropper tip to any surface, as this may contaminate the contents. Advise patients that a single bottle of PROLENSA should be used to treat only one eye.

CONCOMITANT USE OF CONTACT LENSES

Advise patients to 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.

CONCOMITANT TOPICAL OCULAR THERAPY

If more than one topical ophthalmic medication is being used, the medicines should be administered at least 5 minutes apart.
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INDICATIONS AND IMPORTANT SAFETY INFORMATION
Rx Only

ATTENTION: Reference the Directions for Use for a complete listing of Indications and Important Safety Information. INDICATIONS: The TECNIS® 1-Piece Lens is indicated for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed by extracapsular cataract extraction. These devices are intended to be placed in the capsular bag. WARNINGS: Physicians considering lens implantation should weigh the potential risk/benefit ratio for any conditions described in the TECNIS® 1-Piece IOL Directions for Use that could increase complications or impact patient outcomes. The TECNIS® 1-Piece IOL should not be placed in the ciliary sulcus. PRECAUTIONS: Do not reuse, resterilize, or autoclave.

ADVERSE EVENTS: In 3.3% of patients, reported adverse events of cataract surgery with the 1-Piece IOL included macular edema. Other reported reactions occurring in less than 1% of patients were secondary surgical intervention (pars plana vitrectomy with membrane peel) and lens exchange (due to torn lens haptic).

*Compared against AcrySof® IQ (SN60WF), HOYA AF-1™ FY-60AD and enVista® IOLs (MX60).


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Leading Innovation
Transformative technology. Reliable outcomes.

High-Quality Vision
Unmatched image contrast.1* Outstanding visual acuity.

Exceptional Satisfaction
Brodest IOL portfolio. Enhancing each lifestyle.

Bring Vision to Life.

Johnson-Johnson VISION
To the Editor:

I am writing to respond to the January 2019 article, “Amniotic Membrane Use in Pterygium Surgery” (Thomas John, MD). The article contains inaccuracies related to the processing, protein profile, and clinical effectiveness of dehydrated amniotic membrane technologies (such as Ambio Amniotic Membrane Grafts [Katena]).

Dr. John states that dehydration of the amniotic membrane “involves high-temperature processing to remove the water content of the tissue; this has been shown to potentially cause protein denaturation, loss of function and possibly irreparable damage to the tissue, with the possible loss of active components and, hence, their associated biological functions.”

The process employed to clean and dehydrate the Ambio Amniotic Membrane grafts does not expose the native tissue to high temperatures. Additionally, laboratory tests have been conducted to prove that the Ambio graft does contain native growth factors and cytokines. These data were published by Koob et al.1

Dr. John also claims that, when compared to dehydrated amniotic grafts, “cryopreserved amniotic membrane is usually a preferred choice for clinical use in ophthalmology and pterygium surgery.” Ambio grafts have been widely used by eye surgeons since 2002 to treat pterygium and a range of other ocular surface disorders and diseases. According to Katena, more than 125,000 Ambio grafts have been supplied to the ophthalmic surgical community.

I have used both dehydrated and cryopreserved amniotic membrane to treat thousands of patients with pterygium and other forms of ocular surface disease. Both methods of membrane preparation and both types of product work well to preserve the anti-inflammatory, anti-fibrotic properties of this special tissue. There are no published studies that demonstrate the clinical superiority of one preparation method or one product over another. Like many colleagues, I prefer dehydrated amniotic membrane grafts because they can be stored at room temperature for five years. The dry configuration of the tissue also allows for easier cutting, manipulation, placement, and fixation. And finally, the cost of dehydrated amniotic membrane is considerably lower than cryopreserved tissue.

I will appreciate your sharing these facts with your readers to provide more accurate reporting on this topic.

John Hovanesian, MD
Harvard Eye Associates
Laguna Hills, Calif.

Financial Disclosure: Dr. Hovanesian serves Katena as its medical director.


Dr. John responds:

I thank Dr. Hovanesian for his interest in my recent article which reviews pterygia and the best surgical approach in managing them.

As I mentioned in the article, amniotic membrane grafts possess anti-inflammatory and anti-scarring properties that theoretically make it an optimal tissue graft during pterygium surgery. Although the aforementioned is true in general, different processing techniques (e.g., cryopreservation and dehydration) of the amniotic tissue have varying impacts on the biochemical composition and anti-inflammatory properties of the tissue.1 In fact, cryopreservation, but not dehydration, was shown to retain the HC-HA/PTX3 complex, which has been identified as an active matrix component responsible for the observed anti-inflammatory and anti-scarring properties of amniotic tissue.2 This is one potential reason why, in one study, dehydrated amniotic membrane (Ambiodry 2) was not effective in controlling inflammation and scarring in rabbit eyes after extracapsular lens surgery, as the authors of the study mention.3 Hence, despite the presence of some growth factors and the ability to “work well,” dehydrated amniotic tissue lacks the maximal properties that one would expect.

(Continued on page 16)
DEXTENZA is an advancement in steroid treatment

• Resorbable, so no need for removal
• Insert can be removed via saline irrigation or manual expression, if necessary
• Physicians rated DEXTENZA as easy to insert
• Designed to deliver a tapered dose
• Contains fluorescein for visualization
• No additional components or assembly required

INDICATION
DEXTENZA is a corticosteroid indicated for the treatment of ocular pain following ophthalmic surgery.

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS
DEXTENZA is contraindicated in patients with active corneal, conjunctival or canalicular infections, including epithelial herpetic simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, fungal diseases of the eye, and dacryocystitis.

WARNINGS AND PRECAUTIONS
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. Intraocular pressure should be monitored during treatment.

Corticosteroids may suppress the host response and thus increase the hazard for secondary ocular infections. In acute purulent conditions, steroids may mask infection and enhance existing infection.

ADVERSE REACTIONS
The most common ocular adverse reactions that occurred in patients treated with DEXTENZA were: anterior chamber inflammation including iritis and iridocyclitis (9%); intraocular pressure increased (5%); visual acuity reduced (2%); eye pain (1%); cystoid macular edema (1%); corneal edema (1%); and conjunctival hyperemia (1%).

The most common non-ocular adverse reaction that occurred in patients treated with DEXTENZA was headache (1%).

Please see brief summary of full Prescribing Information on adjacent page.
with amniotic tissue. Also, cryopreserved amniotic tissue may be preferred by some surgeons due to its handling properties in the OR; in addition, it’s FDA-recognized as demonstrating anti-scarring and anti-inflammatory functions.²

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Financial disclosure: Dr. John has a small equity interest in, is consultant/advisor to, and has received lecture fees and grant support from Bio-Tissue and Tissue Tech.

Letters to
the Editor

(Continued from page 14)

began on Capitol Hill to investigate why prescription drug prices are rising and how this development is affecting Americans.

Witnesses at the hearing seek to clarify research costs, inflation vs. drug prices, the prescription percentage of patent-protected drugs vs. drug spending, and patent policy regarding the length of time before generic manufacturers can enter into competition.

In testimony, Aaron S. Kesselheim, MD, an associate professor of medicine at Harvard Medical School, stated that the pharmaceutical marketplace is fractured and inefficient.

The solution to this problem involves intelligent legislation and regulation to ensure that U.S. patients and payers pay prices commensurate with the clinical value that the drugs provide,” Dr. Kesselheim said, “and to ensure that even expensive drugs face generic or biosimilar competition after a reasonable and fair time frame.”  

(Continued from page 6)
We are excited to continue into our fourth year of Mackool Online CME. With the generous support of several ophthalmic companies, I am honored to have our viewers join me in the operating room as I demonstrate the technology and techniques that I have found to be most valuable, and that I hope are helpful to many of my colleagues. We continue to edit the videos only to change camera perspective or to reduce down time - allowing you to observe every step of the procedure.

As before, one new surgical video will be released monthly, and physicians may earn CME credits or just observe the case. New viewers are able to obtain additional CME credit by reviewing previous videos that are located in our archives.

I thank the many surgeons who have told us that they have found our CME program to be interesting and instructive; I appreciate your comments, suggestions and questions. Thanks again for joining us on Mackool Online CME.

Richard J. Mackool, MD

MackoolOnlineCME.com MONTHLY Video Series

Episode 39: “My Standard Procedure”
Surgical Video by: Richard J. Mackool, MD

Video Overview:
After posting so many complicated cases, I thought it may be time to review my standard procedure with this one-eyed patient showing some slight macular degenerative changes. Leaving this patient myopic for better reading vision quality, my chopping technique, settings, and the benefits of vacuuming the posterior capsule are all discussed.

Richard Mackool, MD, a world renowned anterior segment ophthalmic microsurgeon, has assembled a web-based video collection of surgical cases that encompass both routine and challenging cases, demonstrating both familiar and potentially unfamiliar surgical techniques using a variety of instrumentation and settings.

This educational activity aims to present a series of Dr. Mackool’s surgical videos, carefully selected to address the specific learning objectives of this activity, with the goal of making surgical training available as needed online for surgeons motivated to improve or expand their surgical repertoire.

Learning Objective:
After completion of this educational activity, participants should be able to:
• Demonstrate and discuss basic techniques of phacoemulsification and cortex removal

Satisfactory Completion - Learners must pass a post-test and complete an evaluation form to receive a certificate of completion. You must listen to/view the entire video as partial credit is not available. If you are seeking continuing education credit for a specialty not listed below, it is your responsibility to contact your licensing/certification board to determine course eligibility for your licensing/certification requirement.

Physicians - In support of improving patient care, this activity has been planned and implemented by Amedco LLC and Postgraduate Healthcare Education. Amedco LLC is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team

Credit Designation Statement - Amedco designates this enduring material activity for a maximum of 0.25 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.
Year three of the Quality Payment Program is here! There are some significant changes to be aware of as you plan what to do in 2019 to earn a bonus and avoid a penalty. Most eye-care providers will be in the Merit-Based Incentive Program, or MIPS. The program’s complexity for year three scoring is much higher since the scoring bar for penalty avoidance was raised to 30 points, which was doubled from the 2018 level. Year one of MIPS had a penalty avoidance of only three points.

What are the four main parts of MIPS and how has the weight of each changed for year three?

The weight of each year-three MIPS component (adding up to 100 percent) is as follows:
- Quality = 45 percent
- Resource Use (Cost) = 15 percent
- Improvement Activities (IA) = 15 percent
- Program Interoperability (PI) = 25 percent.

Program Interoperability might seem like a new MIPS category, but it was renamed mid-2018 by CMS. It was formerly known as Advancing Care Information, but it’s still the electronic medical record portion of MIPS. If you don’t have an electronic medical record system in your practice and have no exemption, your maximum score is limited to 75 points since you can’t score in Program Interoperability.

Two of the categories, Quality and Resource Use, have had their emphases/weighting changed every year since the program’s inception in 2017. In the second year, Quality was worth 50 percent, while the Resource Use category was worth 10 percent.

In some instances, when a provider or group receives an exemption or no score from the Program Interoperability, Improvement Activities or Cost categories, the weight of the category with the exemption or no score is added to the weight of the Quality category. For example, if a practice had a hardship exception for Program Interoperability, then the associated 25 percent would be added to Quality’s 45 percent value, making the new weight 70 percent.

What hasn’t changed for 2019 MIPS?

If you’re considered a small practice (fewer than 16 providers) then CMS retains the IA score-doubling effect. To get 100 percent, you only need to reach half the maximum score of 40. Large practices of 16 or more providers still have to reach 40 points the normal way. Other 2019 MIPS provisions that haven’t changed include the ability to choose to report as an individual, group or virtual group. Additionally, data for Quality and Resource Use is still collected for the entire year, while data for PI and IA is still collected for any 90 or more consecutive days.

As in past years, what you do this year has the potential to affect your Medicare payments two years later; so, the 2019 MIPS component affects 2021 payments. CMS refers to these as the “Performance Year” and “Payment Year.”

What you can do in the coming year to help ensure that your practice earns a bonus—and avoids a penalty.
OMIDRIA® (phenylephrine and ketorolac intraocular solution) 1% / 0.3% is added to ophthalmic irrigating solution used during cataract surgery or intraocular lens replacement and is indicated for maintaining pupil size by preventing intraoperative miosis and reducing postoperative ocular pain.

**IMPORTANT SAFETY INFORMATION**

OMIDRIA must be added to irrigating solution prior to intraocular use.

OMIDRIA is contraindicated in patients with a known hypersensitivity to any of its ingredients.

Systemic exposure of phenylephrine may cause elevations in blood pressure.

Use OMIDRIA with caution in individuals who have previously exhibited sensitivities to acetylsalicylic acid, phenylacetic acid derivatives, and other nonsteroidal anti-inflammatory drugs (NSAIDs), or have a past medical history of asthma.

The most commonly reported adverse reactions at ≥2% are eye irritation, posterior capsule opacification, increased intraocular pressure, and anterior chamber inflammation.

Please see the Full Prescribing Information for OMIDRIA at www.omidria.com/prescribinginformation.

You are encouraged to report Suspected Adverse Reactions to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

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**References:**


10. Matossian C. Clinical outcomes of phenylephrine/ketorolac vs. epinephrine in cataract surgery in a real-world setting. Presented at: American Society of Cataract and Refractive Surgery (ASCRS) Annual Meeting; April 13-17, 2018; Washington, DC.

Q: I reported MIPS via a registry in 2017 and 2018. Have the submission methods changed?

A: No. You can still submit via Claims if you’re a small group, and the Direct EMR and Registry options remain for anyone. If you submit the same MIPS category using multiple methods (for example, if you report Quality via both Claims and Registry), your highest score will count.

Q: For 2018, I’m receiving a small-practice bonus of five points, which will be added to my MIPS Composite score. Is this bonus still available in 2019?

A: The bonus is now six points, but instead of applying that to the Composite score, it all goes to Quality, which has the effect of diluting the bonus points.

Q: Did any of the areas undergo changes I should know about that aren’t noted above?

A: Yes. Both PI and Resource Use changed in significant ways. The 2018 method of reporting PI involved having a “Base” that you had to meet before going to a “Performance” score. That was changed; there’s just one level now. In 2018, there were more than 150 possible PI points, and you only had to reach 100 to max out that category and get 100 percent. For 2019, there are only 100 possible points. There are some bonus points in PI, which can total 10 points, but they are unlikely to be achieved by ophthalmologists, who won’t have prescription drug monitoring programs and opioid treatment agreements. As a result of these changes, getting a perfect score of 100 percent may be more difficult.

For Resource Use, if your office does cataract surgery in an ASC or HOPD, this is the biggest change of all. There’s a new “Episode of Cost” measure which takes into account uncomplicated cataract with intraocular lens surgery and all of the associated costs. At the end of the year, CMS will calculate a normalized value for 66984, which takes into account regional differences, site of surgery and other factors. That value is then multiplied by the number of cases, if you reach the case minimum.

Here are a few important specifics that you should know regarding this change:
- Only items/amounts paid by Medicare for uncomplicated CPT 66984 are counted. Claims to other payers are not part of this; neither are patient-pay, noncovered services such as premium IOLs.
- You need to have been paid for 20 or more 66984 claims to Medicare for 2019 surgery that are not otherwise excluded (see below).
- Anything paid by Medicare related to cataract within a window of 60 to 90 days before the surgery can count.
- All costs paid by Medicare related to the cataract surgery count, which includes all of the related exams, diagnostic tests, reoperations (for example early YAG capsulotomy or IOL repositions, even if not done by the initial surgeon), any drugs used during the surgery or in the office that are separately paid, and anesthesia payments.
- Patients who have concomitant ocular disease which might limit best-corrected visual acuity aren’t counted (such as situations where the patient has a corneal scar or significant posterior segment disease). The Centers for Medicare and Medicaid Services dictates the exclusions by looking at diagnosis codes for the eye that’s having surgery as well as the “time window” above.

The two-step attribution process for “primary-care services,” which was always unlikely to apply to eye doctors, still remains.

If any costs are attributed to a surgeon—or the surgeon’s group, if reporting that way—using either or both of the methods described above, then you are compared to the national norm for cost and scored accordingly. Those who are low-cost would be given a higher Resource Use score. If both two-step and cataract are attributed, each scores in this category. If only one of these applies, then that counts in full for the category. Here, a perfect score would be 10 points on each part scored, which is multiplied by the 2019 weight of 15 percent.

Q: I’ve heard that some medical practices could receive an exemption for some or all of MIPS. Is that true?

A: Yes, if a large natural disaster affects the practice. This was true in both 2017 and 2018 and is likely for 2019, too. However, as we are barely into the year, CMS has not issued any information for 2019 disasters at the time of this writing, since none have occurred.

Those practices who are affected by wildfires or other natural disasters (CMS calls these “extreme and uncontrollable circumstances”) are likely to be given a “pass” on part or all of 2019 MIPS reporting and will therefore receive no penalty in 2021 unless they are able to and elect to submit MIPS data. CMS automatically identifies these areas by their payment ZIP codes. There are other exemptions published by CMS but they are far less likely to apply to the average practice.

Ultimately, what it comes down to is that 2019 MIPS is more complicated this year, and diligence is warranted in order for your practice to avoid a 2021 penalty.

Mr. Larson is a senior consultant at the Corcoran Consulting Group in San Bernardino, California. He can be contacted at plarson@corcoranCG.com.
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Monitoring IOP at Home: A Work in Progress

Now that technology has made home IOP measurement feasible, doctors are beginning to uncover its real-world pros and cons.

Sharon F. Freedman, MD, Durham, N.C.

As physicians managing patients with glaucoma, we face numerous practical challenges. One of them is accurately monitoring intraocular pressure. Most of us only get to check our patients’ pressures every few months in the clinic, which is far from ideal, since we know that pressure fluctuates over time.

It’s no secret that researchers are striving to make 24/7, high-tech IOP-monitoring a reality. That technology will bring us new challenges, including figuring out what to do with the enormous amount of data it will produce for every patient. But in the meantime, it’s possible to improve on our current, sparse supply of data by asking selected patients to monitor their pressure at home. This offers the possibility of getting several readings each day over a period of weeks or months—enough information to make us aware of what’s happening to our patient outside of the office without drowning us in data points.

Home monitoring of IOP is still in its early stages, but as a pediatric glaucoma specialist, I now have several years of experience using rebound tonometry in clinic and at home with young patients. I believe my experience with childhood glaucoma can help to shed some light on the challenges and benefits that lie ahead when this technology becomes more widely used—hopefully in appropriate adult glaucoma patients as well as children.

Benefits of Home Monitoring

The theoretical advantages of having IOP measurements taken outside the office are not hard to see:

• A more accurate measurement of peak IOP. The variability of IOP over time sometimes surprises us; occasionally, the pressure we measure in the office is very different from the previous visit. So it shouldn’t be a surprise—and it has been my experience—that multiple measurements taken outside of the office frequently reveal much higher pressures than we measured in the office.

• Catching pressure fluctuations. It’s been shown that pressure fluctuations—even those measured during periodic office visits—are associated with progression in adult open-angle glaucoma. (This stands in contrast to patients whose IOPs are at target and stable.) We also know that pressure fluctuations can happen outside of office hours. Measuring IOP over a larger range of time offers the possibility of catching those fluctuations.

That raises another point:

• Some fluctuations caused by surgery can be dangerous when they’re not carefully monitored. Sometimes the treatments we provide—including surgery—cause dramatic IOP fluctuations. In the pediatric world, situations prone to such fluctuations might include doing angle surgery and having a little blood in the eye; putting the child on steroids; or putting in a Baerveldt drainage device where we purposely tie the tube off, knowing that it’s going to open when the stitch dissolves. In the latter situation, the pressure may be very high until the stitch dissolves; then it may drop very low. In the adult world, some MIGS procedures are also associated with pressure spikes.

If IOP is being monitored at home during such high-risk times in vulnerable patients, we’ll know when there’s an abrupt pressure change that
Indication

INVELTYS (loteprednol etabonate ophthalmic suspension) 1% is indicated for the treatment of post-operative inflammation and pain following ocular surgery.

Important Safety Information

INVELTYS 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. 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.

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. 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 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.

In clinical trials, the most common adverse drug reactions were eye pain (1%) and posterior capsular opacification (1%). These reactions may have been the consequence of the surgical procedure.

Please see Brief Summary of Prescribing Information for INVELTYS on the next page.
INVELTYS™ (loteprednol etabonate ophthalmic suspension) 1%, for topical ophthalmic use

BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE
INVELTYS is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

CONTRAINDICATIONS
INVELTYS 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.

WARNINGS AND PRECAUTIONS
Intraocular Pressure (IOP) Increase—Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, as well as 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.

Cataracts—Use of corticosteroids may result in posterior subcapsular cataract formation.

Delayed Healing—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.

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.

Viral Infections—Use of 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).

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.

Contact Lens Wear—The preservative in INVELTYS may be absorbed by soft contact lenses. Contact lenses should be removed prior to instillation of INVELTYS and may be reinserted 15 minutes following administration.

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.

Clinical Trial Experience—Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The most common adverse drug reactions in the clinical trials with INVELTYS were eye pain and posterior capsular opacification, both reported in 1% of patients. These reactions may have been the consequence of the surgical procedure.

USE IN SPECIFIC POPULATIONS
Pregnancy—Risk Summary: INVELTYS is not absorbed systemically following topical ophthalmic administration and maternal use is not expected to result in fetal exposure to the drug.

Lactation—Risk Summary: INVELTYS is not absorbed systemically by the mother following topical ophthalmic administration, and breastfeeding is not expected to result in exposure of the child to INVELTYS.

Pediatric Use—Safety and effectiveness in pediatric patients have not been established.

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

NONCLINICAL TOXICOLOGY
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 \textit{in vitro} in the Ames test, the mouse lymphoma thymidine kinase (tk) assay, or in a chromosome aberration test in human lymphocytes, \textit{or in vivo} in the single dose mouse micronucleus assay.

For a copy of the Full Prescribing Information, please visit www.INVELTYS.com.

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US-INV-1800055 December 2018
Home Rebound Tonometry for Pediatric Glaucoma

IOPs tended to be higher in the mornings and lower in the evenings for both normal and glaucoma patients. (Flemmons, Hsiao et al. 2011)

needs to be addressed.

• **Fever concerns about patients missing office visits.** Patients who need to have their pressure checked sometimes can’t come to the office when, or as often, as we’d like. For a patient measuring IOP at home, some office visits purely for IOP checks might actually be unnecessary.

• **A single in-office diurnal curve measurement may not tell the whole story.** It’s helpful to measure a diurnal pressure curve over the course of a day in the clinic (if the patient can manage this), but some studies have shown that in adults the diurnal fluctuation may not be exactly the same from one day to the next.

What’s Taking So long?

Despite the promise of home IOP monitoring, a number of obstacles have caused this idea to get off to a slow start. The first obstacle has only recently been overcome: Having available technology that can safely be used by patients at home.

Most tonometers aren’t suited to home tonometry because they require anesthetizing the cornea. Any physician will be reluctant to let a patient use an anesthetic at home, because if the eye is anesthetized for a home-based reading, there’s a risk that the person taking the pressure will injure the cornea. Neither person would know anything had happened until the anesthetic wore off.

Tonometers that can accurately measure IOP at home without topical anesthetic are not common. In theory, parents could use an air puff device of some type to take the readings, but most patients—young or old—don’t enjoy that experience. In fact, the lack of multiple FDA-approved options for home IOP monitoring is largely the result of the fact that most IOP-measuring technologies don’t lend themselves to home use.

In my experience, the only technology that can easily be used to measure pressure without an anesthetic at home—at least for now—is rebound tonometry, because it touches the eye so gently. I first became interested in this technology when a colleague mentioned a new tonometer that didn’t require a topical anesthetic. In the pediatric world, that’s huge, by the time you put in the topical anesthetic and the child has had a meltdown, you’re starting from scratch, convincing the child to let you check the pressure. Even the Tonopen, which has been the standby for pediatric patients, often proves challenging to use in young children for the same reason.

The first rebound tonometry I tried was the TAO1i from Icare, the company’s first model; our early studies were conducted using that device. It provides a reliability index with each reading and it’s pretty easy to use, but it doesn’t store any data. The next model, the ic100, has a display on it and a few extra bells and whistles. The Icare Pro version (not commercially available in the United States) has storage capability and can be used upright or flat, so you could use it on a patient lying down, making it feasible for use in the OR.

Recently, the Food and Drug Administration approved the Icare HOME model, designed specifically to allow an older patient to use it on himself, thus making home IOP measurement feasible. The device knows whether you’re measuring the left or right eye, and it has a red-light-green-light display that lets patients know when they’re at the right distance from the instrument and the device is angled correctly. When the patient is finished taking a reading, it shows either a repeat indicator or a checkmark, so the patient knows when it’s time to do the other eye. (Notably, it doesn’t let the patient see the pressure reading.)

If the reading was reliable, the machine will store the data, including which eye was measured, the date and the time, the reliability index and the measured pressure. Currently, the device has to be plugged in to a computer to upload the data, but the company plans to upgrade the software to allow the device to wirelessly upload data to the cloud, where it would theoretically be downloadable by anyone with appropriate permission to access it.

Obviously, there will be other technologies that can be used by the patient at home—including high-tech options such as contact-lens-based monitors like the Triggerfish—in the future. I chose to study rebound tonometry because it was available and well-suited for this type of application.
Getting Our Questions Answered

Because the idea of home IOP monitoring was relatively new, we set out to answer some key questions. Initially, we wanted to find out what rebound tonometry could and couldn’t do when used in the clinic, so we conducted a study in the clinic involving 71 children with known or suspected glaucoma. We all of these children could tolerate Goldmann applanation, allowing us to compare the applanation and rebound tonometry IOP readings in a masked fashion. We found that the TAO1i usually read higher than Goldmann, by a little more than 2 mmHg. Occasionally the readings would be significantly different, for reasons we couldn’t determine; we never found one specific thing, such as corneal thickness, that might explain this. We also noted that the device didn’t hurt the cornea. When we stained the cornea, we couldn’t even tell that it had been used.

Next, we set out to see whether families could use the Icare (original model) for home tonometry in children. We studied it under a research protocol with 17 affected children (17 eyes) and 11 normal siblings. We found that caregivers obtained reliable readings 70 percent of the time. The data showed that daily IOP fluctuation occurred in both groups, and the pressures tended to be higher in the morning and lower in the evening. (See graph, p. 26.) Perhaps most significant, peak IOPs were sometimes much different from those measured in the clinic. In five subjects (31 percent) the peak IOP measured at home was more than 6 mmHg higher than that measured in the clinic. This caused us to alter our management of several of these patients, meaning we either performed surgery or changed medications.

Long-term Use at Home

Next, we wanted to know how long we needed to send a device home in order to catch pressure spikes. To get an answer, we examined data from seven children (average age: 9) enrolled to do home rebound tonometry three times a day for more than 30 days. On average, the monitoring lasted for about six months. The parents entered the data into an Excel spreadsheet or used our online entry form. Ultimately, we found that two weeks of monitoring in the children caught more than 90 percent of all pressure spikes, so we concluded that two weeks might be a good minimum length of time to have a child’s pressure monitored if the goal was specifically to find a pressure spike on a given treatment regimen.

We also were able to monitor the impact of our treatment, especially relating to surgical intervention in this small group of childhood glaucoma patients. On average, surgery lowered pressure by 10 mmHg. Perhaps most interesting, we found that the mean variation in pressure over the course of a day decreased when we improved aqueous outflow. Before the intervention, the average daily pressure fluctuation in those eyes was 8 mmHg; after surgery it was 5 mmHg. So not only did we lower the pressure by an average of 10 points, we also decreased the amount of daily variation. This is important because smaller daily variation in pressure is associated with a better visual outcome.
Open your eyes to what’s on the horizon in dry eye.

Sign up for updates at TearCare.com

TearCare is indicated for the application of localized heat when the current medical community recommends the application of a warm compress to the eyelids. Such applications would include Meibomian Gland Dysfunction (MGD), Dry Eye, or Blepharitis.

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pressure fluctuation.

One situation in which we found ongoing monitoring at home to be especially useful was following the implant of a Baerveldt drainage device, when we ligated the tube to prevent early hypotony. That turned out to be valuable for several reasons:

• First, we found that if we added steroids or surgery while the tube was ligated, the pressure usually went up before it went down. (This was not a surprise, but it was useful to know that the data confirmed our expectations.)

• We saw tremendous variations in pressure while we were waiting for the tube to open, sometimes prompting unplanned therapy changes for unusually high IOPs caught at home.

• Perhaps most useful, the parents could precisely pinpoint the moment when the tube opened because the measured pressure would drop. It’s important to know when this has happened because as soon as the tube opens and the pressure plummets, the patient needs to stop using the glaucoma drops for a while or the pressure could get dangerously low.

Knowing when the tube has opened is especially important in some patients, such as those with Sturge-Weber-associated glaucoma, where there’s a choroidal hemangioma in the eye along with the glaucoma. Kids in this situation may get choroidal effusions—leakage from the choroidal hemangioma—and even serous retinal detachments if they have a dramatic pressure drop. If we can more precisely monitor the pressure as it’s changing, we can help to mitigate some of that. For that reason I now routinely use home monitoring in this situation.

Convinced that home IOP monitoring of selected childhood glaucoma patients was helpful in their care, we were interested in exploring attitudes towards home tonometry, both from our patients and our colleagues who treat childhood glaucoma. To that end, we recently sent a survey to 83 parents (or the patients themselves, if they had been treated as children but were now adults), and pediatric ophthalmologists and glaucoma specialists who care for kids with glaucoma. Eighty-four percent of the parents said they were very interested in using this technology; most felt it would improve their physician’s ability to monitor their glaucoma. Eighty percent of the surgeons who responded to our survey indicated interest and saw the potential benefit for patient care, but only 14 percent were actually using any form of home tonometry, demonstrating that this approach to IOP monitoring is by no means widespread.

We also asked doctors in which situations they’d use home tonometry. Most physicians said they’d use it to try to catch IOP peaks or fluctuations that they suspected were occurring, either because readings were inconsistent or they couldn’t do enough clinic visits to be sure. Some said it might help them provide better postoperative care. Overall, most physicians felt there would be a benefit to using home tonometry in selected patients.

Barriers to Use

Despite its potential, a number of barriers to widespread use of home tonometry remain:

• Managing the information. One of the challenges that comes with implementing any kind of home tonometry is processing the resulting data. How do you collect it and make sense of it? How do you make sure you haven’t missed something?

• Opening up new areas of liability. When the patient is being measured at home, who is responsible for interpreting and responding to those measurements, and by what methodology?

• Cost to the physician/practice. Physicians and offices would have to spend money to own or rent the devices, to care for the devices, to train patients to use the devices, and to process all of the data. Currently, there are no treatment codes that would allow physicians to be reimbursed for these costs, although nothing would prevent them from renting the equipment to the patient.

One related thing we discovered is that patients get very attached to using the instrument! They (or their families) often don’t want to give it back. To make home tonometry feasible, one needs to own several (or more) of these devices—at a non-trivial initial cost. Fortunately, through generous support from Saving Kids’ Sight, we’ve been able to purchase several dozen tonometers to loan out (again, under IRB protocol). We’ve now reached out to several other institutions, sharing our protocol and tonometers, to help expand the reach of our Icare Lending Library Project.

• A lack of supporting evidence, especially in adult populations. There’s some evidence in the literature that this technology can be helpful when managing children, and my own experience supports that. However, as far as I know, there’s little published in the adult glaucoma literature demonstrating improved outcomes as a result of measuring pressures at home. I think that such supporting evidence will be needed to increase interest and the use of home tonometry for adult glaucoma patients.

The bottom line is that home tonometry is not likely to sweep the field of glaucoma in the near future. In fact, I suspect most busy clinicians will not want to do this except under select circumstances.

Onward and Upward

Studies involving home tonometry are now appearing in the literature, and some doctors are already using
the Icare Home. Although this is currently mostly used in pediatric populations, the studies indicate that there’s interest in home tonometry in the adult world as well. Nevertheless, I think we’re quite far from widespread implementation at this point. And that may be reasonable. Based on our experience, home tonometry is not appropriate for every patient, nor is it necessary.

In the meantime, the technology continues to improve, and I believe the future for home monitoring is bright, for many reasons. The instruments are getting more user-friendly, and cloud-based storage of data is now on the near horizon. I can imagine a situation in the future in which electronic medical record systems will be able to seamlessly download and integrate the IOP measurements, much as can be done today with home telemetry for arrhythmia monitoring. Perhaps the device could even have an alarm that would alert the patient that her pressure is high and ask whether she remembered to use her drops, thus improving adherence.

In addition, once this technology becomes easy to use and is implemented in more practices, it may actually save doctors time by eliminating the need for patient visits that happen primarily just for a pressure check. Of course, once we have proof that this technology improves outcomes, we’re going to need some kind of reimbursement. And we’ll need to do a lot more research to find out which patients it can help the most, and how best to implement it.

In the meantime, our experience and data so far relate to caring for a very tiny subset of glaucoma patients—kids with childhood glaucoma. The rest of the iceberg, of course, is the adult community. I wouldn’t presume to tell doctors dealing with adult patients how or whether to use home tonometry, but I suspect that what we’re doing with kids is of interest to those doctors who are managing adults. Yes, implementing this technology in an adult practice with a large number of patients could be more daunting than what I’m dealing with, but I’m hopeful that our experience can act as a starting point for studies involving adults.

Dr. Freedman is a professor of ophthalmology and pediatrics and chief of the Pediatric Ophthalmology and Strabismus Division at Duke Eye Center in Durham, North Carolina. She reports no financial ties to Icare or its products.


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Warnings and Precautions

- **Endophthalmitis** may occur following any intraocular surgical procedure or injection. Use proper aseptic injection technique when administering LUXTURNA, and monitor for and advise patients to report any signs or symptoms of infection or inflammation to permit early treatment of any infection.

- **Permanent decline in visual acuity** may occur following subretinal injection of LUXTURNA. Monitor patients for visual disturbances.

- **Retinal abnormalities** may occur during or following the subretinal injection of LUXTURNA, including macular holes, foveal thinning, loss of foveal function, foveal dehiscence, and retinal hemorrhage. Monitor and manage these retinal abnormalities appropriately. Do not administer LUXTURNA in the immediate vicinity of the fovea. Retinal abnormalities may occur during or following vitrectomy, including retinal tears, epiretinal membrane, or retinal detachment. Monitor patients during and following the injection to permit early treatment of these retinal abnormalities. Advise patients to report any signs or symptoms of retinal tears and/or detachment without delay.

- **Increased intraocular pressure** may occur after subretinal injection of LUXTURNA. Monitor and manage intraocular pressure appropriately.

- **Expansion of intraocular air bubbles** instruct patients to avoid air travel, travel to high elevations or scuba diving until the air bubble formed following administration of LUXTURNA has completely dissipated from the eye. It may take one week or more following injection for the air bubble to dissipate. A change in altitude while the air bubble is still present can result in irreversible vision loss. Verify the dissipation of the air bubble through ophthalmic examination.

- **Cataract** Subretinal injection of LUXTURNA, especially vitrectomy surgery, is associated with an increased incidence of cataract development and/or progression.

Adverse Reactions

- In clinical studies, ocular adverse reactions occurred in 66% of study participants (57% of injected eyes), and may have been related to LUXTURNA, the subretinal injection procedure, the concomitant use of corticosteroids, or a combination of these procedures and products.
The most common adverse reactions (incidence ≥ 5% of study participants) were conjunctival hyperemia (22%), cataract (20%), increased intraocular pressure (15%), retinal tear (10%), dellen (thinning of the corneal stroma) (7%), macular hole (7%), subretinal deposits (7%), eye inflammation (5%), eye irritation (5%), eye pain (5%), and maculopathy (wrinkling on the surface of the macula) (5%).

Immunogenicity
Immune reactions and extra-ocular exposure to LUXTURNA in clinical studies were mild. No clinically significant cytotoxic T-cell response to either AAV2 or RPE65 has been observed. In clinical studies, the interval between the subretinal injections into the two eyes ranged from 7 to 14 days and 1.7 to 4.6 years. Study participants received systemic corticosteroids before and after subretinal injection of LUXTURNA to each eye, which may have decreased the potential immune reaction to either AAV2 or RPE65.

Pediatric Use
Treatment with LUXTURNA is not recommended for patients younger than 12 months of age, because the retinal cells are still undergoing cell proliferation, and LUXTURNA would potentially be diluted or lost during the cell proliferation. The safety and efficacy of LUXTURNA have been established in pediatric patients. There were no significant differences in safety between the different age subgroups.

Please see a brief summary of the US Full Prescribing Information on the following pages.


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Dystrophy. Forty of the 41 subjects received sequential subretinal injections of LUXTURNA. Following the injection, patients should be monitored to permit early treatment of any infection. Advise patients to report any signs or symptoms of infection or inflammation without delay.

5.2 Permanent decline in visual acuity
Permanently decline in visual acuity may occur following subretinal injection of LUXTURNA. Monitor patients for visual disturbances.

5.3 Retinal abnormalities
Retinal abnormalities may occur during or following the subretinal injection of LUXTURNA, including macular holes, foveal thinning, loss of foveal function, foveal deshielding, and retinal hemorrhage. Monitor and manage these retinal abnormalities appropriately. LUXTURNA must not be administered in the immediate vicinity of the fovea. [See Dosage and Administration (2.3) in full prescribing information]

Retinal abnormalities may occur during or following vitreoretinectomy, including retinal tears, epiretinal membrane, or retinal detachment. Monitor patients during and following the injection to permit early treatment of these retinal abnormalities. Advise patients to report any signs or symptoms of retinal tears and/or detachment without delay.

5.4 Increased intraocular pressure
Increased intraocular pressure may occur after subretinal injection of LUXTURNA. Monitor and manage intraocular pressure appropriately.

5.5 Expansion of intraocular air bubbles
Instruct patients to avoid air travel, travel to high elevations, or scuba diving until the air bubble formed following administration of LUXTURNA has completely dissipated from the eye. It may take one week or more following injection for the air bubble to dissipate. A change in altitude while the air bubble is still present can result in irreversible vision loss. Verify the dissipation of the air bubble through ophthalmic examination.

5.6 Cataract
Subretinal injection of LUXTURNA, especially vitrectomy surgery, is associated with increased incidence of cataract development and/or progression.

6 ADVERSE REACTIONS
The most common adverse reaction incidence (incidence ≥5%) were conjunctival hyperemia, cataract, increased intraocular pressure, retinal tear, dellen (thinning of the corneal stroma), macular hole, subretinal deposits, eye inflammation, eye irritation, eye pain, and maculopathy (wringling on the surface of the macula).

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of other products and may not reflect the rates observed in practice.

The safety data described in this section reflect exposure to LUXTURNA in two clinical trials consisting of 41 subjects (81 eyes) with confirmed RPE65 mutation-associated retinal dystrophy. Forty of the 41 subjects received sequential subretinal injections of LUXTURNA to each eye. One subject received LUXTURNA in only one eye. Seventy-two of the 81 eyes were exposed to the recommended dose of LUXTURNA at 1.5 x 10^12 vg. 9 eyes were exposed to lower doses. A total of 25 subjects (60 eyes) from Study 1 (n=12) with open-label, dose-exploration safety study. Study 2 (n=29) was on a-label, randomized, controlled study for both efficacy and safety [see Clinical Studies (14) in full prescribing information]. The average age of the 41 subjects was 17 years, ranging from 4 to 44 years. Of the 41 subjects, 25 (61%) were pediatric subjects under 18 years of age, and 23 (56%) were females.

Twenty-seventy of 27 (41.6%) subjects had ocular adverse reactions that involved 46 injected eyes (46/81, 57%). Adverse reactions among all subjects in Studies 1 and 2 are described in Table 1. Adverse reactions may have been related to LUXTURNA, the subretinal injection procedure, the concomitant use of corticosteroids, or a combination of these procedures and products.

Table 1. Ocular Adverse Reactions Following Treatment with LUXTURNA (N=41)

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Subjects n=41</th>
<th>Treated Eyes n=81</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any ocular adverse reaction</td>
<td>27 (66%)</td>
<td>46 (57%)</td>
</tr>
<tr>
<td>Conjunctival hyperemia</td>
<td>9 (22%)</td>
<td>9 (11%)</td>
</tr>
<tr>
<td>Cataract</td>
<td>8 (20%)</td>
<td>15 (19%)</td>
</tr>
<tr>
<td>Increased intraocular pressure</td>
<td>6 (15%)</td>
<td>8 (10%)</td>
</tr>
<tr>
<td>Retinal tear</td>
<td>4 (10%)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>Dellen (thinning of the corneal stroma)</td>
<td>3 (7%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Macular hole</td>
<td>3 (7%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Subretinal deposits*</td>
<td>3 (7%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Eye inflammation</td>
<td>2 (5%)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>Eye irritation</td>
<td>2 (5%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Eye pain</td>
<td>2 (5%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Maculopathy (wringling on the surface of the macula)</td>
<td>2 (5%)</td>
<td>3 (4%)</td>
</tr>
</tbody>
</table>

* Transient appearance of asymptomatic subretinal precipitates inferior to the retinal injection site 1-6 days after injection.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary: Adequate and well-controlled studies with LUXTURNA have not been conducted in pregnant women. Animal reproductive studies have not been conducted with LUXTURNA. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

8.2 Lactation
There is no information regarding the presence of LUXTURNA in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for LUXTURNA and any potential adverse effects on the breastfed infant from LUXTURNA.

8.3 Females and Males of Reproductive Potential
No nonclinical or clinical studies were performed to evaluate the effect of LUXTURNA on fertility.

8.4 Pediatric Use
Treatment with LUXTURNA is not recommended for patients younger than 12 months of age because the retinal cells are still undergoing cell proliferation, and LUXTURNA would potentially be diluted or lost during cell proliferation.

The safety and efficacy of LUXTURNA have been established in pediatric patients. Use of LUXTURNA is supported by Study 1 and Study 2 (see Clinical Studies (14) in full prescribing information) that included 25 pediatric patients with RPE65 mutation-associated retinal dystrophy in the following age groups: 21 children (age 4 years to less than 12 years) and 8 adolescents (age 12 years to less than 17 years). There were no significant differences in safety between the different age subgroups.

8.5 Geriatric Use
The safety and effectiveness of LUXTURNA have not been established in geriatric patients. Clinical studies of LUXTURNA for this indication did not include patients age 65 years and over.

17 PATIENT COUNSELING INFORMATION
Advise patients and/or their caregivers of the following risks:

Endophthalmitis and other eye infections: Serious infection can occur inside of the eye and may lead to blindness in such cases there is an urgent need for management without delay. Advise patients to call their healthcare provider if they experience new eye pain, eye redness, or changes in vision.

Permanent decline in visual acuity: Permanent decline in visual acuity may occur following subretinal injection of LUXTURNA. Advise patients to contact their healthcare provider if they experience any change in vision.

Retinal abnormalities: Treatment with LUXTURNA may cause some defects in the retina such as a small tear or a hole in the area or vicinity of the injection. Treatment may cause thinning of the central retina or bleeding in the retina. Advise patients to follow up with their healthcare provider on a regular basis and report any symptoms, such as decreased vision, blurred vision, flashes of light, or floaters in their vision without delay.

Increased intraocular pressure: Treatment with LUXTURNA may cause transient or persistent increase in intraocular pressure. If untreated, such increases in intraocular pressure may cause blindness. Advise patients to follow up with their healthcare provider to detect and treat any increase in intraocular pressure.

Expiration of intraocular air bubbles: Advise patients to avoid air travel, travel to high elevations, or scuba diving until the air bubble formed following administration of LUXTURNA has completely dissipated from the eye. A change in altitude while the air bubble is still present may cause irreversible damage.

Foveal dehiscence: Advise patients that following treatment with LUXTURNA, they may develop a new cataract, or any existing cataract may get worse.

Shedding of LUXTURNA: Transient and low-level shedding of LUXTURNA may occur in post-surgical tears. Advise patients and/or their caregivers on proper handling of waste material generated from dressing, tears, and nasal secretion, which may include storage of waste material in sealed bags prior to disposal. These handling precautions should be followed for up to 7 days following LUXTURNA administration.

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Refining Postop Infection Prevention

Christopher Kent, Senior Editor

There are many ways—new and old—to prevent post-surgery inflammation and endophthalmitis. Surgery always comes with some amount of risk, and removing a cataract is no exception. Postoperative inflammation—and more concerning, endophthalmitis—are potential consequences that cataract surgeons go to great lengths to prevent. Today, with technology advancing rapidly, new options for preventing these undesirable outcomes are appearing. Nevertheless, many surgeons are hesitant to abandon current protocols, and some surgeons say that many effective low-tech precautions are still frequently overlooked.

Here, surgeons share their experience and advice regarding how to do the best possible job of preventing postoperative inflammation and endophthalmitis—whether or not you’ve adopted any of the cutting-edge protocols.

To Drop or Not to Drop?

The biggest debate right now centers around how to manage the patient at the end of surgery and into the postoperative period. Although giving the patient a battery of preop and postop eye drops has been the standard approach for a number of years, there are two clear arguments for switching to an injection of antibiotic (and possibly other drugs) at the conclusion of surgery: First, evidence is mounting that injecting antibiotics is effective at preventing postop infection—possible more effective than having the patient use drops. Second, drops are a huge burden for the patient and the practice, so the fewer drops the patient has to use, the better.

“Don’t expect to reduce your risk of endophthalmitis by having the patient use antibiotic drops for a week before, or two weeks after, surgery,” says Robert M. Kershner, MD, MS, FACS, professor and chairman of the Department of Ophthalmic Medical Technology at Palm Beach State College, and president and CEO of Eye Laser Consulting in Palm Beach Gardens, Florida. “There’s not a single study showing that this has any substantive effect. The only solid evidence that shows antibiotics to be of any benefit is when they get inside the eye at the time of surgery. In addition, there’s a moderate amount of evidence that suggests that using postoperative antibiotic drops in addition to an intraoperative intracameral or intravitreal injection may lower the incidence of endophthalmitis, compared to using injections or eye drops alone. So it’s probably best to use a combination.”

“We’re at the forefront of a huge paradigm shift in postoperative drug...
delivery,” says Cynthia Matossian, MD, FACS, founder and chief medical officer of Matossian Eye Associates, and a clinical assistant professor of ophthalmology (adjunct) at Temple University School of Medicine in Philadelphia. “By eliminating drops, we’re going to take compliance out of the patient’s hands. We’ll eliminate the confusion and difficulty of managing the drops, and decrease the burden for the patient and the patient’s family. In addition, we’ll be putting the drugs closer to the target tissue.

“The average cataract patient in the United States is in his or her late 60s or early 70s,” she notes. “Managing a complicated schedule of drops can be very challenging for some patients. For example, a steroid drop is tapered over a period of several weeks; an antibiotic drop is stopped earlier than the steroid and the NSAID. A brand-name NSAID is used once a day, but if the pharmacist substitutes a generic drop, it may be used four times a day. This creates a lot of confusion—and this is just the first eye. After a few weeks we do eye two, which has a different schedule that’s not aligned with whatever remains for eye one.

To complicate matters, some patients are forgetful. They may be confused; they may have arthritis in their hands and not be able to squeeze the bottle appropriately; they may contaminate the tip; and they may think they put the drop in when it actually ended up on their forehead or eyelid.

“In addition, the cost of the drops is becoming prohibitive,” she continues. “The cost can be as much as $400 or $500. With higher deductibles and a greater percentage of responsibility being placed on the patient by insurance carriers, patients are experiencing sticker shock when they go to pick up their drops. And when they have sticker shock, guess what they do? They call our offices and yell at our staff. They believe we’re the cause of the high prices, even though we have nothing to do with it. Furthermore, when the pharmacist substitutes generic drops, the frequency protocol changes; that confuses the patients even more, so they call us to get clarification. Aside from having unhappy patients, the number of incoming calls about these issues is becoming burdensome. Dealing with upset patients, tying up our phone lines and technician time, is a cost to the practice.

“For all of these reasons,” she concludes, “minimizing the drop-instillation regimen is the way to go.”

Going Intracameral

“There’s good evidence from multiple studies around the world that intracameral injection of antibiotics is effective, many American surgeons are hesitant to switch to this protocol. Dr. Mamalis points out that one reason many surgeons haven’t switched is that there’s no drug that’s FDA-approved for this purpose.

Dr. Mamalis believes that preoperative povidone iodine is much more effective at ensuring sterility than preoperative antibiotics. “There’s very good evidence that 5% povidone iodine is helpful,” he says. “So, when patients are in the preop holding area we give them a drop of topical povidone iodine. However, it’s important to do this before giving the patient any lidocaine gel to anesthetize the surface of the eye. If you put the gel in first, it will prevent the povidone iodine from spreading out and covering the surface of the eye as it should. Once the patient is in the OR undergoing prep for surgery, the skin is prepped with 10% betadine, but we also put another drop of the 5% betadine on the surface of the eye. By this point the gel has been in the eye for 10 or 15 minutes and has dissipated a bit, so it doesn’t interfere with the coverage of the iodine.”

——CK

Making the Preop Period Count

It’s fairly common for cataract surgeons to put their patients on drops prior to surgery, but many surgeons are questioning the value of that protocol. Nick Mamalis, MD, a professor of ophthalmology and director of ocular pathology at the University of Utah in Salt Lake City, says he hasn’t found the use of antibiotic drops prior to surgery to make a significant difference in the incidence of postop endophthalmitis. “We’ve had issues getting patients to be compliant with the use of drops preoperatively, so we don’t start anything until the patient arrives at the surgery center,” he says.

“After they arrive, patients get three sets of a fourth-generation fluoroquinolone, like moxifloxacin or gatifloxacin, several minutes apart, while they’re receiving dilating drops and topical NSAIDs,” he says. “We include the NSAID because there’s some evidence that having an NSAID onboard before making your incisions will decrease the breakdown of the blood-aqueous barrier in the anterior chamber during cataract surgery. In fact, if the patient has an increased risk of inflammation after surgery—for example, if the patient has a history of uveitis or inflammation in the eye—we’ll often start the patient on NSAID treatment up to a week prior to surgery to reduce the chance of a breakdown of the blood-aqueous barrier.”

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Infection Prevention

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¹ Schanzlin, Olkowski, Coble, Gross. NuLids II Study, April 2018

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“Surgeons would prefer to have an approved postoperative antibiotic that comes in a single-use vial, specifically made for injection following cataract surgery for prevention of endophthalmitis,” he says. “A lot of people have said that without this, they’re concerned about the formulation and how you get it made. I think that’s keeping many surgeons from switching. I’m lucky to be at a university, because we have our own pharmacy. They’ll put a preservative-free antibiotic into a syringe for us under sterile conditions, so we can just inject it directly. Without that advantage, surgeons have to find an outside source on their own.”

Even some surgeons who have switched to intracameral antibiotics are still using postoperative drops as a safety measure. Dr. Mamalis admits he hasn’t committed to eliminating postoperative antibiotic drops yet, despite his use of an intracameral antibiotic. “I’m not sure if it’s because we’re creatures of habit, or simply still worried about postoperative endophthalmitis, but we use a belt-and-suspenders approach,” he says. “We use the intracameral antibiotic but also have the patient use a topical fourth-generation fluoroquinolone for a week postoperatively. I think this is reasonable, because we don’t know for sure whether there might be a problem several days after the surgery. I prefer to err on the side of caution.”

Sheri Rowen, MD, who practices at NVision Eye Centers in Newport Beach, California, and is a clinical assistant professor of ophthalmology at the University of Maryland, notes that even though there is telling evidence throughout the world supporting the postop injection of antibiotics, she hasn’t seen any long-term studies confirming the efficacy of this approach.

“We’ve seen some debate about which antibiotic can be used, and some cases of hemorrhagic occlusive retinal vasculitis (HORV) have occurred,” she points out. “Many surgeons using this protocol are injecting non-preserved moxifloxacin, but a lot of people are trying other alternatives internationally. When we’re at American meetings and we raise hands to see who’s using this approach, it’s not a compelling majority of cataract surgeons yet—at least in the U.S.”

Dr. Mamalis notes that the American Society of Cataract and Refractive Surgery has put together a research council to conduct a series of research studies that could potentially lead to FDA approval of an intracameral antibiotic. “A study like this could only be done through a large group with a large number of surgeons involved,” he says.

“The first project we’re tackling is a masked study comparing an intracameral injection of a fourth-generation fluoroquinolone to topical drops for prevention of endophthalmitis,” he explains. “Because endophthalmitis is rare, we’ll need to enlist as many as 75,000 patients. But if this study proves that an injection of intracameral antibiotic is efficacious, it will allow companies to get approval to make a preservative-free antibiotic for single use after cataract surgery. This will go a long way toward making surgeons more willing to use an intracameral antibiotic.”

Can We Go Dropless?

Dr. Matossian says she’s been doing everything possible to avoid giving the patient postoperative drops for the past two years. “At the conclusion of cataract surgery, just before I seal the incision, I put a steroid and antibiotic combination into the anterior chamber with a 25-ga. bent cannula,” she explains. “I use Dex-Moxi, which is dexamethasone and moxifloxacin; it’s clear, like water. Once it’s placed inside the eye, I seal the incision in the normal way.” Dr. Matossian notes that the downside to her current approach is that neither version of Dex-Moxi (one from Imprimis, one from Ocular Sciences) is FDA-approved. “The combination drugs are manufactured by a 503-A or -B pharmacy,” she explains. “We order it per patient, and the formulation is sent to the ASC.”

Dr. Matossian adds that she still has patients use an NSAID once a day postoperatively. “That’s far easier for the patient than the multi-drop protocol,” she points out. “The exception is if I’ve done a limbal relaxing incision. In that situation the patient also needs topical antibiotics, which I prescribe b.i.d. for five days. In addition, if it was a complex case in which I went in and out of the eye more than normal, or I used a pupil dilating device or the case was prolonged, I might add a topical steroid for just a few days in addition to what I’ve placed intracameral.”

Dr. Mamalis acknowledges that few or no postoperative drops would be good for both patients and practices. “The problem is that there’s not enough data out there for us to really know how well this works,” he says. “In addition, there’s no commercially available approved medication to inject for this purpose. That means you have to go through a compounding pharmacy to get the medication made.
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up. Furthermore, you can’t just put it in the anterior chamber; you have to leave a depot of this medication in the eye, either placing it through the zonules or in the anterior vitreous.”

Dr. Rowen says she thinks the jury is still out on how surgeons will use intracocular antibiotics. “Everybody’s trying to figure out exactly what they’re comfortable with and what they feel they need,” she says. “If you haven’t had a case of endophthalmitis in 20 years, you might feel like you’re doing OK with your current protocol. I think if anything new will be adopted, it will be an intracameral injection done at the end of the case—but I can’t tell you what the majority of doctors will do. There’s no consensus yet. We all want to be in line with the accepted standard of care, but I don’t know that we have an accepted standard of care in this area.”

Stop Infection Before It Starts

Dr. Kershner emphasizes something that’s often omitted from the discussion: If a postop infection occurs, it started during the surgery. In fact, he points out that the term “postoperative endophthalmitis” is misleading. He says the best way to prevent endophthalmitis is to do everything humanly possible to ensure that sterility is maintained during the procedure, rather than focusing on postoperative fallbacks.

“We’re probably infecting many more patients than we realize,” he says. “Fortunately, in most cases the end result isn’t endophthalmitis. The result may be inflammation that we interpret as a low-grade sterile inflammation, when in fact the postoperative cell and flare is secondary to intraocular organisms. Even if that happens, in most patients with a normal immune system—though not all—receiving intraoperative antibiotics will likely ensure that a contamination doesn’t turn into an inadvertent adverse event.

The best way to prevent endophthalmitis is to make sure sterile protocols are followed to the letter during surgery, including a thorough preoperative scrub.

“The point is that what goes on during the surgery is a lot more important than what happens before or after the surgery,” he says. “Preoperative and postoperative antibiotic drops or injections can minimize the chances of endophthalmitis, but preventing it during surgery makes the most sense. That will always be your best insurance policy.”

Dr. Kershner notes that some ophthalmologists might be lulled into the illusion that contamination is unavoidable, and if an infection occurs an antibiotic will take care of the problem. “Let me disabuse them of that notion,” says Dr. Kershner. “Many times the organism is not identified right away, and a frightening number of bugs are now resistant to most of the antibiotics we’ve used in the past. Surgeons must keep in mind that no amount of antibiotic is going to be a substitute for strict adherence to preoperative and intraoperative attention to sterile technique. All ophthalmologists need to take this into account when deciding what they’re going to do to prevent endophthalmitis.

“In the past, when a patient developed an infection, a team of infectious disease experts would be brought in to examine everything associated with that surgery to determine where the bacteria came from,” he recalls. “With good sleuthing, we usually could identify the source. Normally, the ocular surface is already colonized with a variety of resident surface flora, including the common bacteria Propionibacterium acnes followed by coagulase-negative Staphylococcus, Corynebacterium, Streptococcus sp., Enterococcus sp., and to a lesser extent gram-negative bacteria and fungi. In one case I was made aware of, an eye had become infected with the intestinal microflora Morganella morganii, which is not a common organism to find inside the eye, to say the least. How could an organism get from below the waist into the eye? The answer: poor hygiene. Not on the part of the patient, but a member of the surgical team.

“The infectious disease team came in and swabbed everything, including all body parts of the patient and everyone who was in the OR,” he continues. “In this instance, the patient didn’t carry the organism, but one technician did. Apparently, after multiple cases, the tech went to relieve herself and was not scrupulous enough about thorough washing of her hands, and rescrubbing as if it were the first case of the day.”

Ensuring Sterility

Dr. Kershner points out that there are a number of steps every practice should take to minimize the chance of contamination during surgery. First, policies designed for this purpose should be stated and enforced.

- Make sure your techs understand that they have to be scrupulous about sterility. Dr. Kershner notes that when the patient load is heavy, people may drop their guard. “In many surgical centers, they’re turning over those rooms pretty fast, and it’s easy to skip a step in the preoperative scrub routine, such as rinsing the scrub or using an antiseptic lotion as a substitute for a thorough hand scrub done with antiseptic soap and a brush,” he says. “Of course, the one
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time you don’t do a proper scrub is the one time that you’re going to contaminate the patient and end up with an infection.

- **Create a written protocol describing exactly how every eye should be prepped.** “You should have a written protocol specifying how to properly prep an eye for surgery,” says Dr. Kershner. “I’ve seen all kinds of poor protocol. I’ve seen the OR crew put in a couple of drops of betadine followed by a half-hearted wipe of the eyelids with a cotton swab, and then decide that’s good enough. I’ve seen doctors fail to exclude the eyelashes and eyelid margin from the operative field and then drag instruments over them. These types of mistakes will eventually get you into trouble.

  “In fact, if you want to go after the resident flora, or more importantly, the transient microbial flora, you have to be meticulous about the preoperative preparation of the patient—what touches the eye, what gets into the eye, what gets out of the eye, and how and what is used to assure strict antisepsis,” he continues. “Antisepsis doesn’t work unless the antiseptic agent reaches every surface of the skin, eyelashes, and bulbar, palpebral, perilimbal and fornical conjunctiva, and is left on those surfaces for a significant amount of time.”

- **Take the time to train your techs to follow sterile procedure, yourself.** “I don’t leave technician training to someone else,” says Dr. Kershner. “Maybe they received good training before working with me, maybe they didn’t. But the surgeon is the one who has to make sure everything is done correctly. So, I show my ophthalmic medical technologists, scrub and OR nurses exactly how I expect them to scrub before surgery.”

- **Set an example.** Dr. Kershner says that he always makes sure to follow his protocol to the letter. “I make sure that I’m a good example—that I always scrub properly and for long enough to make a real difference,” he says. “I never scrub halfheartedly and throw on some sanitizing gel as a substitute for a thorough scrub.”

- **Make it clear that being the cause of contamination is grounds for dismissal.** “I explain that if anyone doesn’t follow this routine each and every time, they can look for a job elsewhere,” Dr. Kershner says. “I tell them, ‘If we get a case of endophthalmitis, we’re going to go looking for the culprit, and if it’s you, you’ll lose your job.’”

### Preoperative Pearls

Once the basic rules regarding sterility have been established, these strategies will help ensure that no unnecessary sources of contamination make their way into the OR:

- **Examine the patient preoperatively.** “I’ve always believed that the surgeon should see the patient before the surgery—and not just after the patient has been prepped and is in the OR,” says Dr. Kershner. “Sometimes the surgeon hasn’t seen the patient for weeks. I’ve had patients say they wanted to finish the golf tournament, or go up north and visit the kids and think about surgery; then they call two months later and say, ‘OK, let’s do it.’ If that happens, my staff will tell the patient we have to see him again to re-examine and go over everything. The patient may have developed a cutaneous inflammation or infection—acne rosacea, seborrhea or blepharitis. Perhaps the signs of these were missed during the last examination, but those conditions need to be addressed before contemplating surgery. The patient may now be on antibiotics for some reason, or have recently had dental surgery, or have a pulmonary or urinary infection. It can get pretty expensive and time-consuming to discover this kind of thing at the
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last minute when the patient is in the holding area ready for surgery—not to mention the patient’s disappointment. Or worse, we may put the patient at risk by not discovering it at all.”

- **Look carefully at the patient’s chart.** “As the surgeon, you need to stop before and between cases, take a breath, and look carefully at the history of the patient you’re about to operate on before commencing surgery,” notes Dr. Kershner. “I’ve seen cases in which concerns regarding symptoms and signs were noted in the chart, but the surgeon who reviewed the chart missed them. I’ve reviewed other cases where the surgeon did see the patient prior to surgery, but zoomed in and out without doing a careful exam,” he says. “As a result, the surgeon missed something that could have put the patient at risk. A little time spent in advance of the surgery could make all the difference between an uneventful surgical case and a courtroom.”

- **Check for infections elsewhere in the body.** “Doctors often don’t ask about or check to see if the patient has an infection elsewhere in the body, such as a urinary tract infection,” notes Dr. Kershner. “These individuals have a certain degree of bacteremia; they’re already contaminated. Infections elsewhere can end up becoming systemic infections, and those organisms sometimes can show up in the eye. If these factors are not reviewed by the surgeon, and noted in the patient’s record, then they can be missed.”

- **Train your staff to note potential problems and bring them to your attention.** “I always remind my personnel that if anything is discovered—even at the last minute—I want to hear about it,” he says. “Unfortunately, taking the history is usually relegated to the lowest person on the totem pole, so the person who does ask the right questions may not want to bother the doctor with the information—information that may be critical to the patient’s well-being. Tell your staff: ‘If the patient has a systemic infection, let me know. If the patient just had a boil on his neck lanced, point that out to me.’”

- **Talk to the patient prior to surgery.** Dr. Kershner advises: “Ask the patient: ‘How are you feeling? Have you been sick recently? Have you had any procedures performed, such as dermatological, dental or urinary tract procedures? Have you had a colonoscopy? Are you on any medications that you weren’t on the last time I saw you?’ This is part of our job as doctors. It’s the surgeon who doesn’t take the time to do this before surgery who gets in trouble after surgery.”

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“**It’s critical that your injection be preservative-free and the proper dose.**”

—Nick Mamalis, MD

Dr. Kershner adds that you shouldn’t wear a mask when talking to the patient. “Let the patient see that it’s you, your demeanor and the questions you ask that you’re concerned about his or her welfare,” he says. “Finally, don’t wait until the patient is prepped and in the OR to have this conversation. If that’s the norm for you, think about changing your approach. Talking to the patient in the OR is too late.”

### During the Surgery

These intraoperative strategies will help reduce any chance of infection:

- **Minimize your instrumentation.** “There’s usually no need to put instruments in and out of the eye multiple times during cataract surgery,” notes Dr. Kershner. “Every time you do that you increase the risk that bacteria will get inside the eye.”

“In general, you should always use the minimum number of instruments you can use,” he continues. “This has multiple advantages. First, fewer instruments means less sterilizing and managing of tools before, during and after the procedure. Second, the less often you introduce foreign objects into the eye, the safer the procedure becomes. Third, it’s efficient, meaning it takes less time to complete your surgical task and the patient spends less time under the microscope. That’s important because the less time the procedure takes to complete, the lower the risk that something bad will happen while you’re working in the eye.”

“An efficient and well-executed procedure also translates into faster recovery and a better outcome for the patient,” he continues. “Show me a doctor who uses 15 instruments and takes 20 minutes to do the surgery, and I’ll show you a patient with corneal and macular edema and weeks before they achieve clear vision. Of course, being efficient doesn’t mean you have to rush. Hurrying is never in the patient’s best interest.”

“If you need a special instrument,” he adds, “the tech can easily grab a sterile, sealed blister pack with the additional tool.”

- **Know exactly what you’re injecting.** “It’s critical that your injection be preservative-free, and the proper dose,” says Dr. Mamalis. “If you’re going to inject moxifloxacin, some studies have shown that one-tenth of a cc of preservative-free 0.5% moxifloxacin is safe and nontoxic.”

- **Inject through the side-port incision.** “First of all, make sure that your primary wound is watertight,” says Dr. Mamalis. “Then, at the conclusion of the case, you can make the injection through the side-port incision into the anterior chamber. Injecting through the small, less-than-1-mm side-port incision avoids disturbing
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the main incision.

- **Make sure your wound is absolutely watertight.** “A leaky wound is the most serious risk factor for postoperative endophthalmitis,” notes Dr. Mamalis. “Studies, including some done at our institution, have found that a wound leak increases the risk of endophthalmitis 44 times. Not 44 percent, but 44 times! For that reason, we’re very compulsive about checking this before we leave the OR.

  “To ensure that the wounds are watertight, we hydrate the wound and stab incisions,” he explains. “Then we bring the anterior chamber up to physiological pressure, dry the incisions with a Week-Cel sponge, and put gentle pressure on the eye at the limbus on the opposite side. Under high-power microscopy we make sure there’s absolutely no leak. If there’s any question, you can put a little fluorescein on there and perform a Seidel test. In the uncommon situation that we can’t get the wound to seal, we’ll put in a suture.”

**Two Final Thoughts**

Last but not least, these two strategies will help make sure that you’re giving your patients the greatest chance of an excellent outcome:

- **Accept responsibility for any less-than-ideal outcomes.** Dr. Kershner says this was ingrained in him when he trained as a general surgeon before going into ophthalmology. “We were taught that the surgeon is responsible for everything that happens to the patient,” he says. “If you had an infection postoperatively, it was your fault and most likely secondary to poor surgical technique. The surgeon simply did not blame the patient. Assuming responsibility for any problems that might occur following surgery will ensure that you go the extra mile to prevent every type of contamination that’s within your ability to control.”

- **When new options appear, try them—and share your experience.** “The only way we can really know what works best in our hands is to try it on our patients,” says Dr. Rowen. “We can read how well something worked in an FDA study, but that doesn’t necessarily reflect how well it will work in the real world. I prefer to stick with products that are approved, but once they’re approved, I think it’s important to try them and share what we learn. That’s how we decide what persists in our field.”

Dr. Matossian notes two new products that are FDA-approved that should be available shortly. “One is called Dextenza [Eyepoint]; it’s a 9% dexamethasone intracameral ophthalmic steroid suspension that’s placed under the iris using a 25-ga. bent cannula at the conclusion of cataract surgery,” she explains. “Through its ‘Verisome’ technology, it delivers more steroid at the beginning; then over a 30-day period, it bio-erodes and disappears. Thus, it mirrors our steroid tapering schedule.” This may allow surgeons to eliminate the steroid drop with an FDA-approved alternative.

“The second approved product that should be available soon is called Dextenza,” Dr. Matossian says. “It’s an intracameral insert that contains dexamethasone 0.4%; it’s placed into the inferior punctum like a punctal plug at the conclusion of cataract surgery. It elutes dexamethasone for 30 days to treat postoperative pain. It’s another option that will allow us to eliminate postoperative steroid drops. Of course, there will be some situations in which the punctal anatomy may not be suitable for inserting the Dextenza plug. I think that with experience, we’ll know which product is better suited in specific circumstances.”

She adds that the possibility of skipping an NSAID drop is also on the horizon. “There’s a punctal plug in the pipeline that contains an NSAID that elutes over time, but that’s not available yet; it’s still in clinical trials,” she says. “If that comes out, we could place the antibiotic and steroid in the eye and put the NSAID-eluting plug in the inferior puncta. Or, we could put the NSAID-eluting plug in the superior puncta and put a Dextenza plug in the inferior puncta. Either way, the procedure would be totally dropless, postop.”

Dr. Rowen adds that new loteprednol nanoparticle formulations are now available in drop form. “Those include Inveltys 1% ophthalmic suspension [Kala Pharmaceuticals] and Lotemax sub-micron ophthalmic gel 0.38% [Bausch + Lomb],” she says. “These have novel formulations and are designed to work for a longer time than previous modalities.”

Dr. Kershner points out that ophthalmologists—like people in general—tend to be resistant to trying new things. “It’s difficult to get doctors to change their habits, even when the proof that they should is staring them in the face,” he says. “Doctors like to make decisions based upon their clinical experience, but their clinical experience is often not based on real data. If surgeons have always done it a certain way and it seems to be working, then they don’t change. But ophthalmologists need evidence-based studies for doing what they do.”

“Surgeons should be constantly re-evaluating their protocols to see if there’s a better way to do things,” he adds. “Review the literature. Go to the meetings. Look at what other surgeons are doing. Just because you’ve always done it that way doesn’t mean you should continue to do it that way.”

**Review**

Drs. Kershner and Mamalis report no financial ties to any product discussed. Dr. Rowen has consulted for Bausch + Lomb, Kala, Sun Pharma and Eyepoint. Dr. Matossian is a consultant for Eyepoint, Ocular Therapeutics, Ocular Sciences and Imprimis.
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Today, cataract surgeons have more options than ever. They have multiple ways of making a capsulotomy, attacking the nucleus and even controlling miosis during surgery. The results of this year’s cataract surgery survey may give you a clearer picture of how some of your colleagues are adopting these new methods. This year, for example, a slightly higher percentage of surgeons than in previous years say they’re giving femtosecond a try; some are still hesitant to dive into intraoperative wavefront aberrometry; and quadrant division is the preferred way to break up a cataract.

These are just some of the results from this year’s survey on cataract surgery. This month, 2,001 surgeons of the 12,509 who received the survey opened it (16 percent open rate) and, of those, 110 fully completed the survey. To see how your preferences jibe with theirs, read on.

**Femto Use Creeps Up**

This year, a slightly higher percentage of respondents said they use the femtosecond laser for some phase of their cataract surgeries. Thirty-nine percent of the surgeons say they use the femtosecond (up from last year’s 36 percent), and 1 percent (one surgeon) says he uses the Zepto capsulotomy device. Among the femto users, it’s used most commonly to create the capsulorhexis (chosen by 37 percent). The popularity of its other uses appears in the graph on the facing page. The surgeons who use this technology say they appreciate the precision, and its usefulness in certain cases.

A surgeon from Pennsylvania lists what he likes about the technology: “Lower phaco energy, great astigmatism correction (especially with-the-rule) and a good patient experience,” he says. An ophthalmologist from Louisiana agrees, saying, “Femto is safer, creates a more precise capsulotomy and allows the management of mild astigmatism. Femto is essential for a very dense nuclear sclerotic cataract and I will use it in 100 percent of these cases, regardless of reimbursement.”

Kerry Hunt, MD, of Raleigh, North Carolina, says he thinks the femto is most useful in complicated cases. “I do like the ‘perfect’ capsulorhexis but I don’t need it for that,” he says. “Fragmentation is not possible in the most difficult cases where it would ideally be the most helpful. I think it’s greatest utility is in the setting of zonulopathy to get a good rhexis.”

Other surgeons are less impressed...
by femtosecond technology, for a variety of reasons, including the high cost. “It’s useful for capsulorhexis for mature white cataracts,” says a New York surgeon. “Otherwise I do not find it valuable as compared to my standard technique. Time and expense are significant issues as well.” William E. Holcomb, MD, from Cullman, Alabama, needs to see more data. “There is no peer-reviewed evidence showing that either device improves clinical outcomes vs. a procedure performed by a good, experienced cataract surgeon,” he says. A surgeon from Oregon feels similarly. “Femtosecond cataract surgery and Zepto are solutions looking for a problem,” he says. “[It’s] more expense to be borne by the ambulatory surgery center and the patient without demonstrable benefit.”

“I have performed [femtosecond cataract surgery] in the past but no longer do it,” says a surgeon from Missouri. “I found it cumbersome. Positioning of the incisions was problematic at times. I also had two episodes of posterior capsule rupture due to gas buildup behind the cataract.”

### Breaking up the Nucleus

One of the primary areas where the art and science of cataract surgery come together is in the fragmentation of the nucleus. Many surgeons have their own particular way of attacking it that they feel works best for them.

On this year’s survey, the most popular nucleo-fracture technique was quadrant division, chosen by 41 percent of the respondents. The next two most popular techniques were phaco chop (19 percent) and stop-and-chop (18 percent). All of the techniques chosen appear in the graph on p. 48.

“It’s simple, and I can use it on all grades of cataracts,” says a quadrant-division proponent from New Jersey. Alan Baribeau, MD, a surgeon from San Antonio, also likes the mechanical benefits of the technique: “It controls the fraction and phaco-ing best for the wide range of cataracts I have in my practice,” he says.

Several surgeons like the safety of quadrant division. “It works very well without passing instruments posterior to the lens equator,” an Arizona surgeon avers. “It puts less stress on the capsule zonules,” adds a doctor from Ohio.

Surgeons who prefer phaco chop say they use it because it minimizes the phaco power used in the eye. “[I like] the speed of the nucleus disassembly and low ultrasound energy into the eye,” says Ivan Mac, MD, Charlotte, North Carolina, who uses phaco chop. A surgeon from Utah is thinking along the same lines: “It allows almost all the ultrasound to be expended at the iris plane or below, and wastes no energy with unnecessary...”

### Management of Pre-existing Astigmatism

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<tr>
<th>Procedure</th>
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<tbody>
<tr>
<td>Toric IOL</td>
<td>52%</td>
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<tr>
<td>Glasses or contact lenses</td>
<td>12%</td>
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<tr>
<td>Toric IOL plus entry wound on the steep axis</td>
<td>11%</td>
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<tr>
<td>Toric IOL plus AK incisions</td>
<td>8%</td>
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<td>Toric IOL plus AK incisions and an on-axis entry wound</td>
<td>7%</td>
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<tr>
<td>Entry wound on the steep axis plus femtosecond astigmatic keratotomy</td>
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<td>Entry wound on the steep axis plus manual limbal relaxing incisions</td>
<td>3%</td>
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<tr>
<td>Placing the clear corneal entry wound on the axis of astigmatism</td>
<td>2%</td>
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<td>Postop refractive procedure</td>
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sary, inefficient sculpting,” she says. “One can adjust fragment size to density. I prefer cross-action vertical chop with circumferential disassembly for brunescent nuclei.”

“Phaco chop allows me to perform my cases with minimal phaco energy and minimal stress on the cornea,” says Robert Bullington Jr., MD, of Phoenix.

Ben Hasty, MD, of Panama City, Florida, details his technique: “Phaco chop works in soft and hard lenses, and uses familiar tools, with the Seibel chopper already used as a ‘finger.’ ”

For the stop-and-chop adherents, the safety and stability of the technique are important to them.

“Debulking the nucleus with the central trough decreases overall cumulative dispersed energy, and helps protect the endothelium by allowing better control of chopped pieces,” says Alabama’s Dr. Holcomb. A Connecticut surgeon agrees, saying, “It’s easiest to perform efficiently with little energy.”

“I like to see the tip of the instrument at all times,” says an Illinois ophthalmologist. “I cannot do that with horizontal chop.”

**Tackling Cylinder**

As in previous years, the most popular way surgeons correct astigmatism is with toric intraocular lenses, chosen by 52 percent of the respondents (53 percent in 2018). The second most popular choice was glasses and contact lenses (12 percent), followed by the combination of a toric IOL and the entry wound on the steep axis (11 percent). The full range of options selected by surgeons appear in the graph on p. 47.

A Pennsylvania surgeon likes the toric IOL’s predictability in certain cases. “It’s most predictable for moderate or severe astigmatism,” he says. “I generally use femto [AK] for mild astigmatism.” Eileen Wayne, MD, Moline, Illinois, agrees that “it’s very accurate.” Gregory Cox, MD, of Hamilton, New Jersey, calls toric IOLs “accurate and predictable.”

“The toric IOL is safe, reliable and predictable,” says Dr. Holcomb. “I’ll use it if the preop keratometric cylinder is 0.75 D or greater against-the-rule, or 1.25 D or greater with-the-rule.” Greensboro, North Carolina, surgeon Karl Stonecipher also shares his protocol: “For 0.75 D or less I do on-axis incisions and laser astigmatic incisions,” he says. “For 1 D or more I do toric IOLs.”

“I have generally seen very good to excellent results using this technology,” says Phoenix’s Dr. Bullington.

As for the tried-and-true options of spectacles and contact lenses, surgeons say it’s usually a matter of price. “Patients don’t want to pay for a toric lens,” says Christopher Papp, MD, of South Lyon, Michigan, who adds that he does provide toric lenses and limbal relaxing incisions for some patients who, presumably, are willing to pay for them.

**Items of Interest**

Surgeons also weighed in on other aspects of surgery, such as intraoperative wavefront aberrometry and maintaining an adequately sized pupil.

- **Intraoperative aberrometry.** On the survey, a third of the respondents use this technology to help select an IOL, with 11 percent deeming it...
excellent, 13 percent saying it’s good,
8 percent calling it fair and 0.9 percent
(one surgeon) saying that it’s poor.

“This technology provides IOL pow-er verification for post-refractive pa-
tients and adds confidence to my deci-
sion-making when choosing premium IOls,” says a surgeon from Missouri.

Dr. Mac says he’s seen an improve-
ment in his results. “I have objective
clinical data that proves an improve-
ment in my refractive clinical out-
comes,” he says.

For the surgeons who only rate it as
fair, they say it hasn’t separated itself
from conventional methods.

“It hasn’t proven to be superior to
calculations from the ASCRS web-
site in my patients,” says Raleigh’s Dr.
Hunt. “I use it only in post-refractive cases to avoid big errors.” A surgeon
from Utah agrees, saying, “Most of the
time there is very little value [to the
technology]. The in-office measure-
ments are good. It is beneficial in post-
refractive cases [however].”

- **Pupil dilation.** Fifty-one percent
of surgeons say they use a mixture of
epinephrine and lidocaine, injected
intracamerally; 21 percent take no ad-
ditional steps; 13 percent use Omidria
(Omeros, Seattle); and 15 percent use
another method of pupil management
(including phenylephrine/lidocaine in-
jecions, Malyugin rings and epineph-
rine in the irrigation bottle).

- **Infection/inflammation pro-
phylaxis.** Here, the most popular
answer was the conventional use of
a topical anti-inflammatory and anti-
biotic postop (48 percent), followed
by the use of a topical antibiotic and a
combined topical mixture of a steroid
and an NSAID (16 percent). Thirteen
percent use another method (usually
some permutation of intracameral
drug combined with a topical drug or
mixture postop). Nine percent use a
combined mixture of antibiotics and
anti-inflammatories, and 7 percent in-
nject a combined antibiotic/steroid. The respondents’ answers appear in the
graph above.

Surgical Pearls

The surgeons also provided their
number-one piece of advice.

“Have the patient’s head in exactly
the right position for their particu-
lar orbital/lid/head/neck configuration
before ever touching the eye,” rec-
ommends Dr. Holcomb. A surgeon
from Utah shares a safety tip: “Don’t
allow the chamber to bounce around,
and prevent both collapse and over-
deepening,” she says.

A couple of surgeons have thoughts
on the removal of cortex: “Remove
subincisional cortex first during I/A
before proceeding to other areas of
cortex,” says a Pennsylvania ophthal-
mologist. And Jeff Whitman, MD,
of Dallas, advises, “Irrigate/aspirate
cortex centripetally—not with radial
pulling.”

Though there are many techniques
a surgeon can use, a doctor from New
York says it’s better to simplify. “Learn
a technique. Perfect it,” he says. “Your
patients will be happy—and so will
you!”

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How to Manage MIGS Complications

Surgeons offer mitigation techniques for common MIGS complications.

The goal of minimally-invasive glaucoma surgery is a noble one: Offer patients with mild or moderate glaucoma an option that can treat their disease without exposing them to the risks associated with more invasive procedures. However, even the best-laid plans can go awry, and you sometimes have to manage MIGS complications.

In this article, surgeons detail what complications could arise during MIGS procedures and offer advice on how to manage them. We’ll start by discussing general complications that can occur across many of the MIGS procedures, regardless of which outflow or inflow source the doctor is tackling. Then we’ll discuss the specific procedures, what each accomplishes, their most common complications and how to manage them.

General MIGS Complications

While MIGS is an effective way to manage glaucoma in some patients,
there are complications associated with each procedure. However, as Robert Noecker, MD, MBA, the director of glaucoma at Ophthalmic Consultants of Connecticut says, "MIGS procedures aren’t problem-free, but they have fewer problems than standard procedures, and these problems are quite manageable. You just have to be aware of the potential issues. If you address them during the procedure or immediately after, then you should be successful."

Common issues associated with MIGS include challenges using a gonioscope, locating the trabecular meshwork, and preventing and managing excess blood reflux.

Since many procedures require the use of a goniolens, Reay Brown, MD, a glaucoma specialist practicing at Atlanta Ophthalmology Associates, says, “Perhaps the most important thing is to absolutely insist that you achieve a good view before you perform one of these procedures.” Dr. Noecker says manipulating a goniolens can be one of the toughest aspects of an angle procedure. “Using the goniolens with your non-dominant hand with the tool in your dominant hand takes getting used to,” he adds. He urges users not to apply too much pressure on the cornea when using the gonioscope, explaining, “Wrinkling is possible, which will further obstruct your view of the angle.”

Dr. Brown remarks that the goniolens is not ideal, and says he’s working to achieve a better and wider view. “You don’t have to hold it in place, which is very helpful,” Dr. Brown says. While he acknowledges gonioscopy technology’s need to improve, he is adamant that it can and will improve.

Locating the trabecular meshwork is another crucial step in performing many MIGS procedures. “It’s very important to learn the anatomy, as all of these procedures require you to place something in a particular location,” says Brian Flowers, MD, a glaucoma specialist and managing partner of Ophthalmology Associates in Fort Worth, Texas. "You can practice viewing the angle in your office by doing a lot of gonioscopy," he says. Dr. Brown suggests staining the meshwork with Vision Blue, saying that he’s found that to be a big help.

Another potential issue to be aware of is blood reflux. Since the main goal of MIGS is to lower IOP, this makes it easier for blood to reflux back into the canal, Dr. Noecker points out. While experiencing some blood reflux can serve as a confirmation that you’re in the right area, Dr. Noecker adds, “It’s like tapping oil, it’s a good thing…however it can become excessive.” In order to prevent or reduce blood reflux, Dr. Noecker says that viscoelastic is helpful. “I like to keep the pressure a little bit on the high side to push back on the blood. Doing this makes it harder for the blood to enter the eye. That usually works quite well. You may have some blood cells floating around, but not a frank hyphema, which would obscure the vision a lot.”

Another more intuitive way to limit blood flow is to minimize trauma to the iris or ciliary body, which can bleed more readily than an area like the trabecular meshwork. “When you do these canal-based procedures you should get a little blood,” says Dr. Noecker. “But if you’re getting a lot of blood, you may have traumatized the ciliary body or the iris.” To combat this, he suggests inflating the entry chamber very wide. “This can help to push the vascular tissues away. Also, keeping the pressure a little on the higher side is helpful in getting a good view and confirming that you’re entering the canal and not getting posterior, where the ciliary body is.”
Moving on to techniques that increase trabecular outflow, these MIGS procedures deal with removing or bypassing part of the trabecular meshwork or Schlemm’s canal in order to increase flow through the conventional outflow path.

- **iStent and Hydrus.** Glaukos’ iStent and iStent Inject can be inserted into Schlemm’s canal, effectively bypassing the trabecular meshwork and creating a path for aqueous humor to move from the anterior chamber into the canal to restore natural outflow. Similarly, Ivantis’ Hydrus can be inserted into Schlemm’s canal; it aims to open the channel so blocked fluid can flow more freely.

  The two procedures have similar challenges: implanting the device fully and managing hyphemas.

  For both the iStent and the Hydrus, it’s possible to inject the device into the wrong location, such as the sclera or the posterior wall. “The issue is making sure it’s placed in the right location,” says Dr. Flowers referring to the Hydrus. However, Dr. Brown notes, “You can tell when it’s stuck because you can’t move it along the canal.”

  “In the case of a superficial implantation, the iStent doesn’t sit properly and the rings are too visible.” Dr. Brown continues, “The fix is to simply pull back, flatten the approach and then it will slide freely along the canal.” Rotating the head farther can help to position the meshwork into an almost vertical position, creating an easy, flat target, surgeons say. “It’s an intraoperative issue; you simply adjust your positioning,” Dr. Flowers says.

  When it comes to managing a hyphema or a microhyphema, it’s important to remember that, because you’re performing a pressure-lowering procedure, blood will flow more readily and you should expect to have to deal with at least some blood reflux, remarks Dr. Noecker. “Rinse out the blood that refluxes when you tap in but at the same time, prevent it from accumulating overnight,” he says. Blood reflux can be common in these procedures, which is why understanding how to manage it is crucial. “You just keep washing it out and eventually it stops,” says Dr. Brown. “I haven’t had a problem with blood postop.”

  Another issue to be aware of is reimbursement. If an insurance company deems a patient’s glaucoma case too advanced, it may deny reimbursement for the iStent or iStent Inject and be more in favor of a procedure that more significantly lowers IOP. “Insurance companies are very strict about denying coverage for patients who have more serious disease,” Dr. Brown says. This is where it can be beneficial to know how to perform multiple MIGS procedures and interpret which will work best for a given patient, depending on the severity of her glaucoma versus how much IOP you are looking to lower, surgeons say.

- **Trabectome.** The Trabectome aims to improve outflow by using electrocautery to ablate a portion of the trabecular meshwork. Complications here sometimes arise as a result of difficulty in maneuvering the device, which might mean less angle access, issues with coordination and potential thermal injury.

  “[The Trabectome] is somewhat cumbersome to use because it’s a little bit big,” says Dr. Noecker. “Since you rely on electrocautery and are therefore using a thermal effect, you have to have some fluid flowing to keep the temperature down. The worst-case scenario is you can burn something you don’t want to burn.”

  As far as avoiding that, Dr. Noecker says technique is important, “The main thing is to have a gentle touch with the gonio lens,” he says. “You can get a wrinkly view, which makes it hard to keep the Trabectome just in that trabecular space. Don’t press down on the cornea to try to get all
Target Within 1-3

With a single injection at the end of cataract surgery, anti-inflammatory efficacy begins as early as day 1 and continues through day 30.*

- The percentage of patients who received DEXYCU (517 mcg) who had anterior chamber cell clearing on day 8 was 60% (n=94/156) vs 20% (n=16/80) in the placebo group.
- The cumulative percentage of subjects receiving rescue medication of ocular steroid or nonsteroidal anti-inflammatory drug (NSAID) at day 30 was significantly lower in the DEXYCU (517 mcg) treatment group (20%; n=31/156) compared to placebo (54%; n=43/80).1

*DEXYCU was studied in a randomized, double-masked, placebo-controlled trial. Patients received either DEXYCU or a vehicle administered by a physician at the end of the surgical procedure. The primary endpoint was the proportion of patients with anterior chamber cell clearing (cell score=0) on postoperative day 8.

INDICATION AND USAGE
DEXYCU™ (dexamethasone intraocular suspension) 9% is indicated for the treatment of postoperative inflammation.

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
Increase in Intraocular Pressure
- Prolonged use of corticosteroids, including DEXYCU, 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.

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 corticosteroids.

Exacerbation of Infection
- The use of DEXYCU, as with other ophthalmic corticosteroids, is not recommended in the presence of most active 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 disease of ocular structures.
- Use of a corticosteroid in the treatment of patients with a history of herpes simplex requires caution and may prolong the course and may exacerbate the severity of many viral infections.
- Fungal infections of the cornea are particularly prone to coincidentally develop with long-term local steroid application and must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate.
- Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection.

Cataract Progression
- The use of corticosteroids in phakic individuals may promote the development of posterior subcapsular cataracts.

ADVERSE REACTIONS
The most commonly reported adverse reactions occurred in 5-15% of subjects and included increases in intraocular pressure, corneal edema and iritis.

Please see brief summary of full Prescribing Information on adjacent page.

References:
1. DEXYCU™ (dexamethasone intraocular suspension) 9% full U.S. Prescribing Information. EyePoint Pharmaceuticals, Inc. December 2018.

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1 INDICATIONS AND Usage
DEXYCU (dexamethasone intraocular suspension) 9% is indicated for the treatment of postoperative inflammation.

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS

5.1 Increase in Intraocular Pressure
Prolonged use of corticosteroids including DEXYCU 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.

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 corticosteroids.

5.3 Exacerbation of Infection
Employment of a corticosteroid medication in the treatment of patients with a history of herpetic simplex requires 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 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 culture should be taken when appropriate.

5.4 Cataract Progression
The use of corticosteroids in phakic individuals may promote the development of posterior subcapsular cataracts.

6 ADVERSE REACTIONS
The following adverse reactions are described elsewhere in the labeling:

- Increase in Intraocular Pressure [see Warning and Precautions (5.1)]
- Delayed Healing [see Warnings and Precautions (5.2)]
- Infection Exacerbation [see Warnings and Precautions (5.3)]
- Cataract Progression [see Warnings and Precautions (5.4)]

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Risk Summary
There are no adequate and well-controlled studies of DEXYCU (dexamethasone intraocular suspension) in pregnant women. Topical ocular administration of dexamethasone in mice and rabbits during the period of organogenesis produced cleft palate and embryofetal death in mice and malformations of abdominal wall/intestines and kidneys in rabbits at doses 7 and 5 times higher than the injected recommended human ophthalmic dose (RHOD) of DEXYCU (517 micrograms dexamethasone), respectively [see Data in the full prescribing information].

In the US general population the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

8.2 Lactation
Risk Summary
Systemically administered corticosteroids are present in human milk and can suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. There is no information regarding the presence of injected DEXYCU in human milk, the effects on breastfed infants, or the effects on milk production to inform risk of DEXYCU to an infant during lactation. The developmental and health benefits of breastfeeding should be considered, along with the mother’s clinical need for DEXYCU and any potential adverse effects on the breastfed child from DEXYCU.

8.4 Pediatric Use
Safety and effectiveness of DEXYCU in pediatric patients have not been established.

8.5 Geriatric Use
No overall differences in safety or effectiveness have been observed between older and younger patients.

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DEX0019
of the air out and get a good view. Pressing the cornea can deflate it. I put viscoelastic on the cornea so that the goniolens can kind of float on that and give you a good view.”

Surgeons say that they can only treat between 90 and 120 degrees using the Trabectome, which, again, makes it important to understand the patient, his specific glaucoma case and IOP-lowering needs. “[The Trabectome] is sometimes not enough to have an impact,” remarks Dr. Brown. “The makers of the Trabectome are trying to make a comeback with some newer designs which may have a role in the future.”

- **Kahook Dual Blade.** This procedure completely removes a strip of the trabecular meshwork in order to increase outflow. “It’s kind of like [the Trabectome],” Dr. Noecker says, “but without the cautery part. It’s very straightforward and it’s a relatively inexpensive device, but you’re limited in how much of the trabecular meshwork you can open in one sitting.” It can involve complications that have already been discussed, such as problems using the gonioscope, accessing more than 120 degrees of the meshwork and dealing with blood reflux.

- **Circumferential trabeculotomy procedures.** This MIGS method lowers IOP by inserting a suture (GATT), or device (Trab360) into Schlemm’s canal, navigating 180 or 360 degrees around the canal, and then performing a trabeculotomy. Complications involve the suture or device getting stuck (which we’ll discuss in the next section), accidentally pulling it out of the canal and dealing with more blood reflux than usual as you remove the meshwork tissue.

Dr. Brown discusses what to do in the case of a device accidentally being pulled out. “Regarding the portion of the catheter that’s outside of the eye, it’s easy for that to get caught on something, or be pulled out. You have to know how to deal with that portion of the catheter,” he says. “In that event you just start over. As you get more experienced, that shouldn’t happen.”

When it comes to blood reflux, Dr. Flowers says, “Each time you do a trabeculotomy you’ll get bleeding. [To manage this], it’s always important when you pierce the eye that you keep it pressurized afterwards. If you have the eye full of viscoelastic, you have to leave it in there for a while to tamp on the blood. Once you rinse the viscoelastic out, immediately make sure that the balanced salt solution goes right in so that the pressure stays above 20 mmHg while the viscoelastic discourages bleeding right afterwards. It’s transient; blood usually goes away within a few days.”

Dr. Brown agrees, saying, “It’s usually managed just by waiting. I’ve never had to re-operate on a patient.”

### ABIC Procedures

An **ab interno** canaloplasty procedure seeks to improve outflow by catheterizing the canal and dilating the natural outflow pathways, including Schlemm’s canal, the trabecular meshwork and the distal outflow system. Complications associated with an ABIC procedure include overinflation of Schlemm’s canal and the device getting stuck.

“Think the main complication could be overinflation of Schlemm’s canal with the Healon,” notes Dr. Flowers. “When you’re doing **ab interno** there are two ways to do it; you can do it with Sight Sciences’ device (the OMNI) which determines for you how much viscoelastic is going to be injected, or you can do it with the Ellex probe (iTrack) where you control how much gets injected.” In regard to Ellex’s iTrack, Dr. Flowers continues, “When you’re doing **ab interno**, you don’t have to worry about a scleral window rupture because you’ve injected too much viscoelastic, so you can inject a little more than you would in an **ab externo** procedure. It’s nice to be able to be a little bit more aggressive, but if you get carried away and overdo it with the injecting, you can create a Descemet’s detachment, which can be an issue.”

Dr. Flowers says that how you manage these complications depends on their location. “If you have a Descemet’s detachment and it’s superior, you can leave a little bit of air in the eye, which will tend to flatten it out,” he says. “Sometimes you can hit it, pop it with a YAG laser and the fluid will leak out. [However] I’ve never had a Descemet’s detachment that ultimately compromised the vision.”

When discussing the propensity for the device to get stuck, Dr. Flowers estimates it happens about 10 percent of the time; however he goes on to explain how to remedy this issue. “If you can’t advance it all the way around, you can do various maneuvers to try to advance it as far as possible,” he says. “A typical maneuver would be to pull back and then advance it again—a back-and-forth motion that breaks through the blockage.” Dr. Flowers offers additional management techniques: “You can put a little external pres-
sure on the eye where the iTrack is,” he says. “You can pull it out one way then turn around and go the other direction. If that doesn’t work, you inject and treat the areas that you can. Think about a circle; if you get a quarter of the way around one way, then halfway around going the other way, at least you can inject those areas and treat three quarters of the eye.”

More specifically, with regard to the OMNI, Dr. Flowers says, “It’s really a combination of canaloplasty and GATT, so it has similar complications.” The OMNI device first catheterizes and viscodilates, then performs a trabeculotomy. In terms of bleeding, Dr. Brown says that since viscodilation is done first, that reduces the blood reflux, both at the time of surgery and postop. “There’s more direct control of what you’re doing in this procedure as it’s less likely for the catheter to get caught on something or to have the tech inadvertently pull it out,” he says. While issues may not be as pronounced as those with GATT or an AbiC procedure, Dr. Noecker says there are things to be aware of. “Don’t do the procedure until the view is great. Pressurize the eye as much as possible during the procedure, which can help enhance the view so that the cornea is not wrinkling and you have a nice clear view of the trabecular meshwork. This also keeps the other structures away from the trabecular meshwork so you don’t traumatize them inadvertently. And the most important thing to prevent bleeding is to make sure the pressure is on the higher side.”

The Promise of MIGS

Many doctors choose to treat glaucoma using medication because trabeculotomies and tube shunts are seen as more aggressive approaches that carry inherent risks despite IOP-lowering efficacy. However, many patients don’t need a dramatic reduction in pressure. Wills Eye Hospital’s Marlene Moster, MD, presented an overview of minimally-invasive glaucoma surgery at the 2014 FDA Workshop in Washington, D.C., “Supporting Innovation for Safe and Effective MIGS.” She estimated that 75 to 80 percent of patients have the ability to control glaucoma symptoms using medication. By undergoing MIGS, patients can decrease their dependency on medication and therefore minimize risks associated with prolonged medicinal use, which include drug side effects, the medications’ financial burden and problems with adherence.

MIGS aims to lower IOP by improving outflow or reducing inflow from an ab interno approach. This can be achieved through bypassing or eliminating the trabecular meshwork, shunting aqueous humor into the suprachoroidal or subconjunctival space or reducing aqueous humor production. MIGS differs from traditional procedures in patient head position, microscopic or gonioscopic view, as well as placement of the surgeon’s hands. There’s minimal trauma associated with MIGS because there’s less disruption to the normal anatomy of the eye, surgeons say. In most instances, this can lead to a quicker postop recovery, possibly allowing patients to resume day-to-day activities after only a short period of time.

MIGS procedures can also be combined in order to achieve higher efficacy. Since there are various ways in which MIGS seeks to lower pressure, should an initial procedure fail or not achieve desired results, a doctor can try another MIGS method. This is why it’s suggested to know how to perform more than one procedure, preferably ones that seek to lower pressure through different paths. Brian Flowers, MD, a glaucoma specialist and managing partner of Ophthalmology Associates in Fort Worth, Texas, suggests learning how to do a Schlemm’s canal procedure and also learning to do some form of gonioassisted transluminal trabeculotomy, or GATT. Learning procedures that lower IOP through different methods, he reasons, can allow you to analyze a patient and decide which MIGS would best suit her specific glaucoma case.

While MIGS isn’t as efficient in lowering IOP as a traditional surgical approach, these procedures can provide modest reduction in pressure, and they continue to show increases in efficacy as MIGS methods and devices advance. MIGS can decrease and, in some cases, completely eliminate the risks associated with traditional surgery, which is why it continues to gain popularity. Reay Brown, MD, a glaucoma specialist practicing at Atlanta Ophthalmology Associates discusses the aims of the procedures. “The goal is to lower the pressure, that’s number one, and number two is to get patients off medication as much as possible,” he says. “That’s also very important and is a great benefit to the patient. Reducing the medication burden is a gain financially, but it also helps with side effects.” Robert Noecker, MD, MBA, the director of glaucoma at Ophthalmic Consultants of Connecticut, says, “It’s a whole new era with these procedures and they’re certainly, as a group, safer than traditional glaucoma surgery.”

—A.S.

Subconjunctival Outflow

Using this technique, IOP is lowered by bypassing the conventional outflow pathway altogether. Here, aqueous humor moves from the anterior chamber into the subconjunctival space, effectively creating a new drainage canal.

* Allergan’s XEN gel stent. Complications associated with inserting this device involve issues with patient facial anatomy, ensuring flow is established and monitoring the patient postop.

"The biggest challenge is the injector itself," Dr. Brown acknowledges. "Especially in the left eye, it can be hard to work over a high
cheekbone.” Similarly, Dr. Noecker notes, “It can be difficult depending on patient anatomy, as you ideally want to get the stent to inject between 11 and 1 o’clock superiorly underneath the eyelid.” In order to manage facial-anatomy complications, Dr. Noecker says, “You can use a second instrument to twist the eye in order to kind of move it away from the bad anatomy site. It takes a little practice, but you can rotate the eye a few clock hours, and then you have space to do the injection.”

For a successful procedure, flow from the anterior chamber into an internal bleb must be established. “You confirm this by increasing the pressure in the eye and washing the viscoelastic out,” Dr. Noecker says. “That’s an important step. Once the device is placed, you want to rinse the eye out and remove all the viscoelastic so that it doesn’t clog the tube. You want to establish that fluid is going through the tube and puffing up the conjunctiva to make a bleb. Then you can be confident in the function of the stent. If you don’t do that, the flow may not start and it’s easier for subconjunctival scarring to begin.”

Since this is a bleb procedure, albeit an ab interno one, there can be cases of leakage and scarring of the bleb in addition to exposure of the tube. For these reasons, Dr. Noecker says that you have to follow patients fairly closely postop. “You need to manage the bleb,” Dr. Brown adds. “It’s important to be able to needle these blebs, which is something not necessary with other internal procedures.” Dr. Noecker points out that, in terms of postop monitoring and intervention, “The good thing is that you can do something. The bad thing is that you have to do it.”

**Aqueous Humor Reduction**

Here, the ciliary body is treated in an effort to lessen the production of aqueous humor and, ultimately, lower IOP.

- **Endoscopic cyclophotocoagulation.** Complications that can occur when performing an ECP procedure include inflammation and problems working with the probe.

  “It’s a whole new era with these procedures and they’re certainly, as a group, safer than traditional glaucoma surgery.”
  — Robert Noecker, MD

Dr. Flowers says that the biggest complication to be aware of with ECP is inflammation. Dr. Noecker agrees, saying, “You tend to get more inflammation because you’re treating the ciliary body. [To manage this] the patient has to be on steroids a little bit more.” Dr. Flowers says intracameral steroids have been a great help. “We used to get fibrin—a protein buildup—in the eye after the surgery,” he says. “But years ago we started using intracameral steroids and it virtually eliminated fibrin. A very robust anti-inflammatory treatment will minimize inflammation complications.”

To avoid further inflammation, Dr. Noecker says, “You have to be careful with the endo probe in the eye so as not to traumatize the iris by either lasering or bumping the iris, because that will lead to a fair amount of inflammation.”

Dr. Flowers has some final tips.

“Make sure that the lens [at the tip of the probe] is clean before it is autoclaved,” he says. “If you leave any debris on the lens of the camera then it’ll get baked on and mess up your view. The lens is very durable so you can wipe it with some force to make sure the tip is clean. Also, when you insert the camera into the eye, make sure you’re in a blood-free zone so you don’t get blood on the tip of it, which would obscure your view.”

**The Future**

MIGS is at the cutting edge of glaucoma surgery; and Dr. Flowers says, “MIGS is here to stay.” Dr. Brown calls it “the greatest breakthrough in glaucoma to come about in [my] 30 years within the industry. The goal now is to increase efficacy so that we’re able to lower pressure in patients who have more advanced disease and higher pressure.”

MIGS is still a relatively new category in glaucoma treatment and while each procedure has its complications, doctors continue to explore management practices as MIGS provides an alternative to medical therapy and more invasive surgery. “We appreciate having these procedures,” Dr. Noecker says. “They aren’t perfect, however, and anything we do involves a little bit of a risk or a downside. However, by knowing the downsides, we can make these surgeries safe and give people good vision quickly while, at the same time, addressing IOP.”

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Dr. Noecker reports financial ties to Glaukos, Ellex, Sight Sciences, BVI and Allergan. Dr. Brown is the chief medical officer for Sight Sciences. Dr. Flowers is a consultant for and does research with Glaukos, Ivantis, Alcon, iStar, InnFocus and Sight Sciences.
A number of exciting, cutting-edge retinal treatments are being investigated against the backdrop of Spark’s Luxturna being approved by the Food and Drug Administration last year. Here’s a sampling of some promising new drugs and gene therapies.

**Next-Generation Anti-VEGF**

According to Pravin Dugel, MD, who is in practice in Phoenix, one of the most exciting drugs in this category is brolucizumab (Novartis), which is a single-strand antibody fragment. “The Phase III trials, HAWK and HARRIER, have shown anatomic superiority over aflibercept. This is the next drug in the pipeline that will change our management,” he says.

The HAWK study included neovascular AMD patients randomized 1:1:1 into three treatment groups: 358 patients received 3 mg of brolucizumab, 360 patients received 6 mg of brolucizumab, and 360 patients received 2 mg of aflibercept (Eylea, Regeneron).1

The HARRIER study included neovascular AMD patients randomized 1:1 into two treatment groups: 370 patients received 6 mg of brolucizumab and 369 patients received 2 mg of aflibercept.1

In both studies, patients in the brolucizumab group received three loading doses and then were treated every 12 weeks during the maintenance phase. Patients in the aflibercept group were treated every eight weeks.

In HAWK and HARRIER, the mean change in best-corrected visual acuity from baseline to week 48 was noninferior for brolucizumab compared with aflibercept. In the HAWK study, brolucizumab patients who received 3 mg experienced a mean BCVA gain of 6.1 letters, and those who received 6 mg improved by 6.6 letters, compared with 6.8 letters for the patients who received 2 mg of aflibercept.

In the HARRIER study, patients who received 6 mg of brolucizumab experienced a mean gain in BCVA of 6.9 letters compared with 7.6 letters in the aflibercept group. Additionally, 57 percent of HAWK patients and 52 percent of HARRIER patients who received 6 mg of brolucizumab were maintained on a 12-week interval after the loading phase until the final end point of week 48.

Another exciting anti-VEGF drug is conbercept, which is made by Kang Hong Biotech from China. “It may be the first drug that’s FDA-approved from China,” Dr. Dugel explains. “It’s a fusion protein with a change in domain IV that will potentially allow it
respectively, at week 20. Five of 48 pa-
squares mean CRT reduction from +10 and +5.3 letters at week 20. Least-
change from baseline was +6.2, +8.3
nibizumab. Least-squares mean BCVA
of abicipar, and 16 patients received ra-
baseline, week four, and week eight
patients who received abicipar experienced intraocular inflammation,
which resolved without sustained vision loss.
Combination Drugs

Several combination drugs are un-
der development. Topping the list is
faricimab, which used to be known
dosed every 12 weeks and 9.6 letters in
patients treated with ranibizumab 0.5
mg dosed every four weeks. Compara-
ble reductions in CRT were also noted in
patients treated with both dosing intervals of faricimab and those treated
with ranibizumab. In STAIRWAY, the
rates of ocular and systemic adverse events observed with faricimab were
similar to those with ranibizumab.
“These results are very encouraging
given the less frequent dosing interval of faricimab,” Dr. Lim says.
Based on these data, Genentech/
Roche will be initiating a global Phase III program for faricimab in wet AMD.
“The LUCERNE Study (Phase III faricimab versus aflibercept) is unique
in its design in that it will explore dif-
ter dose regimens in patients in the first year and then a ‘personalized treatment in-
terval’ from week 60 onward,” Dr. Lim
says. “This will be of great value for the
day-to-day care of patients if the drug
is approved.”

Another promising drug is OPT-302
from Opthea, an Australian company.
“It suppresses VEGF-C and D,” Dr.
Dugel explains. “It would allow for a
pan-VEGF inhibition in combination
with any of the VEGF-A inhibitors
currently available. The early studies
have been very encouraging, and the
Phase III studies are being done in
neovascular AMD and DME.”

There is also the drug previously
known as Luminate. It’s now called
risuteganib from Allegro. “The results
Figure 1. New drugs may slow the progression of geographic atrophy.

to bind better to the target than we’ve
seen before.”

A study was conducted to compare
the efficacy and safety of conbercept
and ranibizumab (Lucentis, Genen-
tech) when administered according to a treat-and-extend (TREX) proto-
col for the treatment of neovascular
AMD in China. The study concluded
that both drugs had equivalent effects in visual and anatomic gains at one
year. Longer treatment intervals were
achieved in more patients in the con-
bercept group.

Allergan’s abicipar pegol is also showing
promise. “It’s a very small drug that
theoretically has great potential and
may have greater durability than any of the drugs that we’ve had so far,” says
Dr. Dugel. “However, the challenge for this drug is that the inflammation rate is very high, 15 percent, so we’re hoping to get more clarity on that.”

In the Phase II trial, abicipar demon-
strated durability of effect. Best-
corrected acuity and central retinal
thickness (CRT) improvements were
similar between abicipar and ranibi-
zmab at weeks 16 and 20 (eight and
12 weeks after the last abicipar injec-
tion and four weeks after the last ranibizumab injection). No serious ad-
verse events were reported.

This multicenter, randomized, dou-
ble-masked comparison included 64
patients who received intravitreal injec-
tions of abicipar 1 mg or 2 mg at baseline, week four, and week eight (three injections) or ranibizumab 0.5 mg at baseline and monthly for five
months.
Twenty-five patients received 1 mg
of abicipar, 23 patients received 2 mg
of abicipar, and 16 patients received ran-
ibizumab. Least-squares mean BCVA
change from baseline was +6.2, +8.3
and +5.6 letters at week 16 and +8.2,
+10 and +5.3 letters at week 20. Least-
squares mean CRT reduction from
baseline was 134, 113, and 131 µm at
week 16, and 116, 103 and 135 µm,
respectively, at week 20. Five of 48 pa-

March 2019 | reviewofophthalmology.com | 59
have been encouraging for diabetic macular edema,” Dr. Dugel says.

Last is a topical agent from Ocu-
lus that contains a cycloheximide plat-
form. It’s currently being studied in
Scandinavia and Eastern Europe, ac-
cording to Dr. Dugel.

Dry AMD/Geographic Atrophy

Apellis has developed a drug to treat
geographic atrophy called APL-2, which
is a complement inhibitor. “It inhibits
the transformation of C3, and the pre-
liminary results have been very
encouraging in slowing down the pro-
geression of geographic atrophy,” Dr.
Dugel says. “However, the downside
is that there seems to be an increased
risk of developing neovascular macular
degeneration. We don’t know why yet,
but Phase III studies are under way.
This is the first time that we’ve seen
something that shows an encouraging
result in geographic atrophy.”

Dr. Lim emphasizes that more data
will be necessary to make a decision
about it. “This increased risk of CNV
may prove to be the limiting factor in
the use of this drug,” she says.

According to Apellis, APL-2 is de-
signed to inhibit the complement cas-
cade centrally at C3, and it may have
the potential to treat a wide range of
complement-mediated diseases more
effectively than is possible with partial
inhibitors of complement.5 APL-2 is a
synthetic cyclic peptide conjugated to
a polyethylene glycol (PEG) polymer
that binds specifically to C3 and C3b,
effectively blocking all three pathways
of complement activation. Interim data
from three trials have demonstrated
meaningful improvements in lactate
dehydrogenase and hemoglobin levels
in previously untreated patients and in
patients who are suboptimal respond-
ers to eculizumab.

Another interesting drug is AKB-
9778 from Aerie. “It is currently be-
ing studied for diabetic retinopathy,”
Dr. Dugel says. “It’s delivered subcu-
taneously, so it goes to both eyes sys-
temically. In previous studies it was
associated with a decrease in progres-
sion of diabetic retinopathy, as well as
improvement in renal function. If any
of these results are duplicated in this
study, I think it will have an enormous
impact, not just because it’s a different
mechanism of action but also because
of its subcutaneous delivery.”

The Phase IIa clinical trial found
that activation of Tie2 by subcutane-
ous injections of AKB-9778 combined
with suppression of vascular endothe-
lial growth factor caused a significantly
greater reduction in DME than that
seen with suppression of VEGF alone,
and similar reductions in the two-step
progression of diabetic retinopathy
were seen compared to ranibizumab
in both eyes.6

Gene Therapy

Luxturna (voretigene neparvovec)
from Spark is the first gene therapy in
ophthalmology to be FDA-approved.
It’s a gene replacement for RPE65 for
patients with retinitis pigmentosa, as
well as Leber’s. “It’s a groundbreaking,
unique treatment that gets to the
heart of the cause of the problem for
this type of retinitis pigmentosa,” says
Dr. Lim. “I think it gives patients hope
where there wasn’t any hope before.
Because these children can now be
cured, they won’t be relegated to a
time of blindness.”

Phase I studies showed potential
benefit of gene replacement in RPE65-
mediated inherited retinal dystrophy.
The Phase III study found that vore-
tigene neparvovec gene replacement
improved functional vision in RPE65-
mediated inherited retinal dystrophy,
previously medically untreatable.7

The open-label, randomized, con-
trolled Phase III trial was conducted
at two sites in the United States in pa-
tients aged 3 years or older with BCVA
of 20/60 or worse and/or visual field
less than 20 degrees in any meridian,
or both, in both eyes, with confirmed
genetic diagnosis of biallelic RPE65
mutations, sufficient viable retina,
and the ability to perform standard-
ized multi-luminance mobility testing
(MLMT) within the luminance range
evaluated. Participants were randomly
assigned (2:1) to intervention or con-
trol. Intervention was bilateral, sub-
retinal injection of 1.5 × 1011 vector
 genomes of voretigene neparvovec, 0.3
mL total volume. The primary efficacy
endpoint was the one-year change in
MLMT performance, measuring func-
tional vision at specified light levels.
The intention-to-treat and modified
ITT populations were included in pri-
mary and safety analyses.

The study included 29 patients who
were randomly assigned to interven-
tion (n=20) or control (n=9). At one
year, mean bilateral MLMT change
score was 1.8 light levels in the inter-
tervention group versus 0.2 in the con-
trol group. Thirteen (65 percent) of
20 intervention participants, but no
control participants, passed MLMT
at the lowest luminance level tested (1
lux), demonstrating maximum possible
improvement.

For treating chronic disease,
RegenXBio has developed RGX-314,
which is being developed as a one-time
subretinal treatment for wet AMD.
It includes the NAV AAVS vector en-
coding an antibody fragment, which
inhibits VEGF, modifying the pathway
for formation of new leaky blood ves-
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IM-0007 Rev C
sels that lead to retinal fluid accumulation and vision loss. In preclinical animal models with conditions similar to macular degeneration, significant and dose-dependent reduction of blood vessel growth and prevention of disease progression was observed after a single subretinal dose of RGX-314.4

“This is an actual anti-VEGF Fab gene put in a specialized virus vector, which is technologically very difficult,” Dr. Dugel explains. "In other words, it's not just a generic virus vector, which is usually AAV2; it's AAV8, which is specialized to go specifically to the retina. And they've been able to show, for the first time, that there is a dose relationship with expression of the protein, which is extraordinarily important. It's the first time we've ever seen that, and the early phase study has been very encouraging. With a higher dose, there's a dose relationship, and there's a decrease in the number of injections and an increase in the visual acuity. But to me, the most important thing is that there is an objective dose relationship in terms of the protein that's produced. I look forward to further results, but also to the next phase in study. If that finding is duplicated in a larger study, it will transition gene therapy from a rare disease treatment into a chronic disease treatment. That will really change everything we do.”

The Phase I clinical trial has enrolled 24 previously treated wet AMD patients who are responsive to anti-VEGF therapy and are 50 years of age or older in four cohorts.8 The study is designed to evaluate four doses of RGX-314: 3 x 10^9 GC/eye; 1 x 10^10 GC/eye; 6 x 10^10 GC/eye; and 1.6 x 10^11 GC/eye. The study will evaluate the safety and tolerability of RGX-314 at 24 weeks after a single dose administered subretinally. Primary endpoints include safety and tolerance. Following completion of the primary study period, patients will continue to be assessed until week 106 for long-term safety and durability of effect.

Dr. Lim is optimistic about the future of retinal therapies. “The future is bright for patients with neovascular AMD and even rarer genetic diseases such as RPE65 RP,” she says. “New drugs with longer duration of action, different molecular targets, combination therapies and even extended drug delivery may be on the horizon. For non-neovascular AMD and geographic atrophy, advances are also occurring. Innovation and scientific discovery will hopefully alleviate the suffering of many of our patients in the near future.”

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Tech Trends in Vitreoretinal Surgery

A look at retinal surgery innovations, from visualization to instrumentation.

Müller Urias, MD, Felipe Pereira, MD, Rodrigo Brant, MD, Rafael Caiado, MD, Antonio Brant Fernandes, MD, Rubens Belfort Jr., MD, PhD, and Mauricio Maia, MD, PhD, São Paulo, Brazil

Over the past five years, our specialty has witnessed several significant changes in the technologies available to us in the operating room. Though these innovations come from different parts of the technology realm, they each aim to improve surgeons’ performance and outcomes. Such innovations include new models of surgical microscopes and smaller, more efficient vitrectomy devices. Looking ahead, robotics will be present in the operating room sooner than we expect and may allow the surgeon to perform delicate tasks without injuring adjacent tissues. Here, we’ll discuss some of the latest inventions.

Visualization

One area that’s made strides in recent years is our ability to visualize retinal procedures. This new point-of-view includes 3-D systems like that from Alcon/TrueVision and real-time, intraoperative optical coherence tomography.

The Ngenuity 3-D system uses a high-dynamic-range camera and a high-resolution 4K monitor. It provides the surgeon with very good image depth and magnification power, while maintaining a wide field of view and comfortable ergonomics for long surgeries. The digital image system and regulation in the aperture of the camera can display a usable image while using lower light intensity, which could mean less retinal phototoxicity for patients. The manipulation of the digital image with the use of different image filters to improve the color and contrast at specific moments during the surgery is another possibility that will be explored in the near future.

One significant benefit of a 3-D viewing system is that it allows the surgeon to teach residents and fellows surgical techniques, since it allows the operating team to see what the surgeon sees (Figure 1). Also, an assistant can help by designating targets and defining paths using a computer mouse.

Many retinal surgeons around the world seem interested in the technology; the latest Preferences and Trends Survey of the American Society of Retinal Specialists in 2018 reported that 15 to 20 percent of surgeons have used the 3-D system and found it useful. Furthermore, 35 to 50 percent said that they plan to purchase the equipment in the future.

Also in the imaging arena, intraoperative OCT has made strides. Systems such as the iOCT (Haag-Streit), EnFocus (Leica) and the Rescan 700 (Carl Zeiss Meditec) can make internal limiting membrane peeling, management of adhesions and visualization of a tractional detachment easier, as well as give a better view of the subretinal space (Figures 2 and 3).

Figure 1. Heads-up surgery may help improve documentation as well as assist in the training of other surgeons.
The advent of swept-source OCT, with its longer wavelength compared to SD-OCT, improved the study of pre- and postoperative retinal status.\(^7\)\(^8\) This characteristic of SS-OCT allows it to visualize through some media opacities and to reduce RPE laser scattering. After macular hole surgery, SS-OCT appears to be a novel way to assess retinal status in a gas-filled vitreous cavity, and provides a high-quality image. Therefore, with an early assessment of macular hole closure, patients may need to be in a face-down position for less time.\(^7\) Certainly, image quality and acquisition latency from devices such as the intraoperative OCT have much to improve. However, there wouldn’t be any innovation without any initial effort.

**Instruments**

Alongside a new view of the procedure are new ways to manipulate the posterior segment’s structures.

- **27-ga. vitrectomy cutters.** The 27-ga. vitrectomy system was introduced in 2010, but, to date, has not been adopted by most retinal surgeons.\(^2\) This is shown by the 2017 ASRS PAT Survey in which about 70 percent of surgeons reported not using it, and 20 percent say they use it for only 5 percent of their cases.

  Despite creating self-sealing incisions and the promise of lower frequency of hypotonia, vitreous prolapse and endophthalmitis, disadvantages such as reduced luminance from a smaller-gauge light probe and worse vitreous aspiration rates may have delayed the widespread adoption of this technology.

  With technological improvements, different light sources such as xenon, mercury vapor or LEDs were introduced. These light sources decreased the risk of phototoxicity while still yielding good illumination. This efficient lighting allows better visualization in 27-ga. surgeries, making the option more attractive to surgeons.

  What’s more, a 3-D surgical viewing system can optimize the illumination of the lower-gauge cutting devices, thanks to the aperture control of the camera and its ability to use less light. Another critical step toward improved efficiency with the 27-ga. system is the use of high-cut-rate technology. With a higher cutting rate, the aspirated vitreous has a lower viscosity, allowing a better rate of aspiration.

  Another recent innovation is two-dimensional cutting. TDC is a technology developed by Dutch Ophthalmic Research Center that features two cutter openings inside the guillotine shaft. This design allows a vitreous cutting action in both the forward and backward movements. The main benefits of this technology include cutting rates of up to 16,000 cpm, increased flow rate and reduced retinal traction. Other companies also use techniques to increase duty cycle and improve system efficiencies, such as the Bi-Blade Dual Port (Bausch + Lomb) and the Hypervit Dual-Blade (Alcon) that can generate up to 20,000 cpm.

  Due to the improvements in the features and safety of the 27-ga. system, the indications for its use have expanded. Today, it can be used in nearly all cases of retinal surgery and it’s especially useful in cases of diabetic retinopathy with multiple areas of fibrovascular proliferation and retinal traction. Thanks to its size, the 27-ga. probe can easily enter small spaces for membrane dissection, reducing the need for bimanual techniques.\(^3\) Despite the companies’ and surgeons’ best efforts, though, the 27-ga. system still has limitations, with reduced stiffness of the instruments and fragile tools for longer complex surgeries.

  Some patients who are receiving...
multifocal IOLs, and who have symptomatic floaters, find their floaters to be more bothersome, and some surgeons feel that vitrectomy is a possible option for these patients. For those cases of floaters in patients with excellent visual acuity, a 27-ga vitrectomy could be a suitable procedure due to the smaller scleral wound and the possibility for reduced leakage. This sutureless procedure may decrease the risk for refractive errors postop and also may reduce the risk of endophthalmitis (Figure 4), though more data on this is required.15

*New models of instruments and vitrectomy cutters.* The latest technology in the field of vitrectomy cutters is the hypersonic probe developed for the Stellaris Elite (Bausch + Lomb), which is available for the company’s 23-ga. system. During vitrectomy, this probe uses hypersonic vibrations that reach about 1.7 million per minute to liquify adjacent vitreous. With this technology, the aspiration port is open at all times, allowing constant aspiration flow and, consequently, greater stability in vitreous removal, even in severe cases such as pediatric vitrectomies.

**Technique Assistance**

In addition to visualization, implementation of technologies in different areas—such as robotics and pharmacology—has enhanced our surgical techniques and could improve surgical outcomes.

Experimental models of robotic instruments have demonstrated that it may be possible to reduce surgeon hand tremor in order to access specific retinal depths precisely—including intravascular spaces. Robotics may also be able to prevent inadvertent retinal touch.13 In addition, a procedure performed by a surgeon-controlled robot—already a reality in surgical specialties such as gastrointestinal surgery and urology—is in a human trial, and has already performed 12 surgeries.10

Currently, one of the possible limitations of this technology lies in the massive number of variables and patterns during surgery that a human can identify and react to faster than the algorithm. There’s also the constant fear of software failure during the operation.

In the realm of pharmacology, research into novel anti-vascular endothelial growth factor agents that could be used before surgery to reduce bleeding; new dyes, such as an açai-fruit extract (Figure 2),11,12 that could be used during the operation to improve the identification of ocular structures; and the development of sustained-release drug implants all show potential to enhance both our techniques as well as visual outcomes. Research is also underway on a new vitreous substitute that may decrease the need for face-down positioning after certain retinal procedures.

**Visual and Retinal Recovery**

Researchers are also investigating ways to assist retinal and/or visual recovery and regeneration. Due to the level of difficulty of these projects, however, their results and numbers are still not statistically robust. However, they’re still very important, since they’re encouraging more studies in their areas. Embryological, genetic and technological projects stand out in the search for retinal and visual recovery.

Embryology has been an exciting tool in retinal recovery, mainly with the use of stem cells (recently covered in the June 2018 Retinal Insider by Peter Bracha, MD, and Thomas A. Ciulla, MD). Currently, however, amniotic transplantation has been questioned as a tool for recurrent macular holes (NCT03528122). The treatment using embryological therapy suffered from lack of safety data until recently, and it’s important to emphasize that such studies should be ethical and conscientiously analyzed, and their results carefully published, to avoid a frenzy from the media and desperate patients.

Providing stronger evidence, at least in specific applications, are genetic therapies, exemplified by Luxturna (voretigene neparvovec-rzyl, Spark Therapeutics). Luxturna’s successful trials, and a more significant number of companies supporting the research, the production cost could possibly be lowered, and the feasibility of this type of treatment could increase.

Another trend in visual rehabilitation is the use of retinal prostheses (reviewed in the June 2017 Retinal Insider by Derrick L. Cheng, MD, David...
There are many technical and scientific reasons why we need harvesting at various times, such as the need to improve our ability to criticize data, document surgery differently, and visualize systems could allow us to believe in "miracle" could make them jump at the nearest study or therapy.

Trends in vitreoretinal surgery go hand-in-hand with scientific evidence. The interplay between technology and techniques can be critical to document surgery differently, and therefore improve our ability to critically analyze each new technological trend as it works its way through the pipeline. In this way, using scientific evidence, surgeons will be able to make the best decisions regarding which new technology to use for their surgeries.

### Table 1. Vitrectomy for Floaters: Quality-of-Life Impact

<table>
<thead>
<tr>
<th>Subscale</th>
<th>Before PPV (median)</th>
<th>After PPV (median)</th>
<th>p-value</th>
<th>No. with improved scores (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General health</td>
<td>75 (50-100)</td>
<td>75 (50-100)</td>
<td>0.157</td>
<td>2 (25)</td>
</tr>
<tr>
<td>General ocular pain</td>
<td>60 (40-80)</td>
<td>80 (60-100)</td>
<td>0.023*</td>
<td>6 (75)</td>
</tr>
<tr>
<td>Near activities</td>
<td>81 (38-100)</td>
<td>81 (63-100)</td>
<td>0.180</td>
<td>2 (25)</td>
</tr>
<tr>
<td>Distance activities</td>
<td>75 (58-100)</td>
<td>100 (75-100)</td>
<td>0.043*</td>
<td>5 (63)</td>
</tr>
<tr>
<td>Social functioning</td>
<td>94 (75-100)</td>
<td>100 (88-100)</td>
<td>0.083</td>
<td>3 (38)</td>
</tr>
<tr>
<td>Mental health</td>
<td>75 (38-81)</td>
<td>94 (50-100)</td>
<td>0.011*</td>
<td>8 (100)</td>
</tr>
<tr>
<td>Role difficulties</td>
<td>88 (25-100)</td>
<td>100 (75-100)</td>
<td>0.042*</td>
<td>5 (63)</td>
</tr>
<tr>
<td>Dependency</td>
<td>100 (58-100)</td>
<td>100 (83-100)</td>
<td>0.102</td>
<td>3 (38)</td>
</tr>
<tr>
<td>Driving</td>
<td>67 (58-67)</td>
<td>92 (75-100)</td>
<td>0.016*</td>
<td>8 (100)</td>
</tr>
<tr>
<td>Color vision</td>
<td>100 (50-100)</td>
<td>100 (100-100)</td>
<td>0.317</td>
<td>1 (13)</td>
</tr>
<tr>
<td>Peripheral vision</td>
<td>75 (50-100)</td>
<td>100 (75-100)</td>
<td>0.059</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>UCVA (LogMar)</td>
<td>0.17 (0.09-0.30)</td>
<td>0.09 (0.00-0.17)</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

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Laser vs. Ranibizumab For PDR Patients

Scientists aimed to identify whether baseline characteristics of eyes with proliferative diabetic retinopathy were associated with better outcomes when treated with panretinal laser vs. ranibizumab in the DRCR.net Protocol S.

Participants had PDR, visual acuity of 20/320 or better, and no previous PRP. Eyes were randomized to PRP or intravitreous 0.5-mg ranibizumab. Here are some of the findings:

- Ranibizumab was superior to PRP for change in visual acuity and development of vision-impairing central-involved diabetic macular edema over two years ($p<0.001$).
- Among 25 characteristics, none in PRP participants were associated with superior outcomes relative to ranibizumab-assigned participants.
- The relative benefit of ranibizumab over PRP in terms of change in VA appeared greater in participants with higher mean arterial pressure ($p=0.03$); without previous focal/grid laser ($p=0.03$); with neovascularization of the disc and elsewhere on clinical exam ($p=0.04$); and with more advanced PDR on photographs ($p=0.02$).
- For development of vision-impairing central-involved DME, the relative benefit of ranibizumab over PRP seemed greater among non-white participants ($p=0.01$) and those with higher mean arterial pressure ($p=0.01$).

Scientists wrote that no identified characteristics were associated with superior outcomes using PRP vs. ranibizumab. They added that their exploratory analyses provides additional support for the premise that ranibizumab might be a reasonable alternative to PRP for PDR over a two-year period.

Retina 2019; Feb. 18 [Epub ahead of print].
Bressler SB, Beaulieu WT, Glassman AR, et al.

The Sleep/Glaucoma Connection

Researchers from the Wilmer Eye Institute at Johns Hopkins University say that a patient's sleep characteristics may play a role in the development of glaucoma.

In this cross-sectional study, the researchers included 6,784 glaucoma patients from the 2005 to 2008 National Health and Nutrition Examination Survey who were age 40 and above and who had completed a detailed sleep questionnaire. Participants were asked such questions as, "How much sleep do you usually get at night on weekdays or work days?" and "How long does it usually take you to fall asleep?" The questionnaire was set up to look at the following predictors:

- sleep duration;
- sleep latency;
- sleep disturbances;
- sleep medication use; and
- daytime dysfunction due to sleepiness.

The outcomes included disc-defined glaucoma (either right or left disc demonstrating glaucoma) and visual field defects (VFD) assessed by frequency-doubling perimetry.

The investigators found that the odds of disc-defined glaucoma were three times higher among subjects who slept for ≥210 hours per night compared with those who slept seven hours per night. The odds of disc-defined glaucoma were two times higher among subjects who fell asleep in ≤9 minutes or ≥30 minutes, compared with 10 to 29 minutes. The odds of VFD were three times higher among subjects who slept for ≤3 hours per night, compared with seven hours per night. The odds of VFD were two times higher among subjects who had difficulty remembering things and three times higher among subjects who had difficulty working on a hobby due to daytime sleepiness compared with those without difficulty.

The researchers say there appear to be associations between glaucoma and abnormal sleep parameters, and that these abnormal sleep patterns may be a risk for, or consequence of, glaucoma.

J Glaucoma 2019;28:97-104
Qiu M, Numah P, Boland M.
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A 12-year-old boy presents to the Wills Eye emergency room with unilateral blurred vision and photophobia.

Connie Wu, MD, James P. Dunn, MD, and Carol L. Shields, MD

Presentation

A 12-year-old Caucasian male with progressive blurred vision, photophobia and pressure-like pain in his right eye presented to the Wills Eye emergency room. Symptoms were noted two days prior when he was playing soccer and had to step off the field due to excessive photophobia of his right eye, which was also red. His left eye was asymptomatic. He didn’t sustain any ocular trauma and was otherwise in his usual state of good health.

Medical History

There was no past ocular history. The past medical history revealed mild intermittent asthma. Family history included glaucoma in his grandmother and a cerebrovascular accident in his grandfather. Social history was negative for recent travel or contact with cats or dogs but included contact with a family-owned farm that raised free-range chickens. He had no known allergies and took no medications.

Examination

On ocular examination, visual acuity was 20/20 OU. Pupils were normal. Intraocular pressure was 30 mmHg OD and 14 mmHg OS. Confrontation visual fields and ocular motility were full bilaterally. The anterior segment examination of the right eye revealed mild injection of the conjunctiva temporally, stellate inferior keratic precipitates, 1+ cell and trace flare, and moderate vitreous cell. The left eye was unremarkable.

On fundus examination of the right eye there was blurring of the nasal margin of the optic disc and a partial macular star without edema. An elevated white retinal lesion with associated subretinal fluid, vitritis, vasculitis and intraretinal hemorrhage, suggestive of an inflammatory mass, was identified in the inferotemporal midperiphery (Figure 1).

What is your diagnosis? What further workup would you pursue? The diagnosis appears on p. 72.
Workup, Diagnosis and Treatment

Imaging of the affected eye with macular OCT (Fig. 2A) revealed disruption of the inner and outer retina with subtle cystic changes and mild vitritis in the temporal macula. OCT through the inflammatory mass in the right eye revealed overlying vitritis, retinitis, choroiditis and subretinal fluid with debris (Figure 2C, D). B-scan ultrasonography (Figure 3) revealed an echodense elevated mass measuring 4.26 mm in diameter by 0.91 mm in thickness. The left macula was normal.

Based on the appearance of the retinal lesion, the patient was diagnosed with Toxoplasma chorioretinitis; the patient and his parents denied any risk factors for exposure including contact with cats or raw meat/unclean foods. He was treated empirically with Bactrim while awaiting serologic testing results. Unfortunately, the first collected sample was inadequate and a second sample had to be drawn after he had already undergone two weeks of treatment. Titers for Toxoplasma IgG were positive at 164 IU/mL, but the IgM was negative. Although it wasn’t possible to confirm active Toxoplasma infection with this particular test, the patient was treated empirically with Bactrim, prednisolone acetate 1% and dorzolamide 2%-timolol 0.5% for intraocular pressure control during the early inflammatory phase. He improved over the course of six weeks.

The differential diagnosis in this young patient with acute onset, unilateral decreased vision and photophobia in the setting of ocular hypertension and an inflammatory retinal lesion included infectious, inflammatory and neoplastic etiologies. Infectious causes included protozoan (e.g., toxoplasmosis), bacterial (e.g., Bartonella, tuberculosis, syphilis, Lyme disease), viral (e.g., mumps, herpes simplex), fungal (e.g., histoplasmosis) and nematodal (e.g., Toxocara). Inflammatory etiologies included juvenile idiopathic arthritis, sarcoidosis, tubulointerstitial nephritis and uveitis syndrome, and inflammatory bowel disease. Less likely malignant etiologies included leukemia, lymphoma and retinoblastoma.

Toxoplasma gondii is a parasitic protozoan thought to be the most common cause of infectious posterior uveitis in the world, infecting about a quarter of the U.S. population and an even greater proportion in other parts of the world. Ocular involvement is estimated at 2 percent in the United States.
States. Following initial ocular infection with *T. gondii*, the recurrence rate is greatest within the following year. Most infections are acquired through ingestion of the oocysts from soil/water or the cyst form from infected meat; only a fraction of cases comprise transplacental transmission.²

We didn’t come across a case report of *Toxoplasma* chorioretinitis from free-range chickens; however, chickens are considered one of the most important hosts in the epidemiology of *T. gondii* infection.³ Free-range chickens are a particularly efficient source of infection for cats who then excrete the environmentally resistant oocysts. Additionally, human consumption of undercooked infected chicken meat may play a role.

*Toxoplasma* chorioretinitis is largely a clinical diagnosis, and while a positive IgG antibody does not confirm the diagnosis, a negative IgG and IgM titer effectively rules it out. Affected individuals often present with unilateral decrease in vision with floaters. Ophthalmic examination typically reveals a posterior or panuveitis, and a subset may have associated elevated IOP.⁴ The classic retinal findings include a necrotizing chorioretinitis with yellow-white inflammatory lesions with blurred margins and focal vitritis, classically described as a “headlight in the fog.” Our case was different in that there was no old chorioretinal scar. Some cases present with a characteristic lobular perivasculitis, thought to be due to vascular endothelial inflammation.

Treatment of ocular toxoplasmosis remains controversial without a clear evidence-based protocol. Left alone, most cases resolve within two months. However, treatment is typically initiated in cases of vision-threatening lesions of the macula or optic nerve and in immunocompromised patients.⁵,⁶ Various combinations of antibiotics and steroids have been studied. There is currently no treatment regimen that definitively improves final visual acuity compared to placebo, but current goals of treatment include shortening the active disease course and reducing recurrence.⁴ A recent double-masked randomized clinical trial found that intermittent antibiotic treatment with Bactrim decreased the risk of *Toxoplasma* retinochoroiditis recurrence up to three years following initial infection.⁶ Additionally, intravitreal injection of clindamycin and dexamethasone may be an acceptable alternative to the classic treatment in ocular toxoplasmosis, as outcomes including visual acuity improvement and vitreous inflammation reduction were comparable to traditional oral agents.⁷

In conclusion, *Toxoplasma* chorioretinitis is a clinical diagnosis with characteristic findings, but clinical history does not always include an exposure to cats. Free-range chickens should be considered in cases of *Toxoplasma* chorioretinitis as a potential vector of disease transmission in cases without feline contact. Treatment is controversial because it hasn’t been shown to alter final visual outcomes, although most clinicians opt to treat severe, vision-threatening cases to shorten the active course and possibly reduce recurrence. REVIEW

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BRIEF SUMMARY:
Consult the Full Prescribing Information for complete product information.

INDICATIONS AND USAGE
Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

 DOSAGE AND ADMINISTRATION
Instill one drop of Xiidra twice daily (approximately 12 hours apart) into each eye using a single-use container. Discard the single-use container immediately after using in each eye. Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.

CONTRAINDICATIONS
Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients in the formulation.

ADVERSE REACTIONS
Clinical Trials Experience
Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in clinical studies of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. In five clinical studies of dry eye disease conducted with lifitegrast ophthalmic solution, 1401 patients received at least 1 dose of lifitegrast (1287 of which received lifitegrast 5%). The majority of patients (84%) had ≤3 months of treatment exposure. 170 patients were exposed to lifitegrast for approximately 12 months. The majority of the treated patients were female (77%). The most common adverse reactions reported in 5-25% of patients were instillation site irritation, dysgeusia and reduced visual acuity. Other adverse reactions reported in 1% to 5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis.

Postmarketing Experience
The following adverse reactions have been identified during postapproval use of Xiidra. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
Rare cases of hypersensitivity, including anaphylactic reaction, bronchospasm, respiratory distress, pharyngeal edema, swollen tongue, and urticaria have been reported. Eye swelling and rash have been reported.

USE IN SPECIFIC POPULATIONS
Pregnancy
There are no available data on Xiidra use in pregnant women to inform any drug associated risks. Intravenous (IV) administration of lifitegrast to pregnant rats, from pre-mating through gestation day 17, did not produce teratogenicity at clinically relevant systemic exposures. Intravenous administration of lifitegrast to pregnant rabbits during organogenesis produced an increased incidence of omphalocele at the lowest dose tested, 3 mg/kg/day (400-fold the human plasma exposure at the recommended human ophthalmic dose [RHOD], based on the area under the curve [AUC] level). Since human systemic exposure to lifitegrast following ocular administration of Xiidra at the RHOD is low, the applicability of animal findings to the risk of Xiidra use in humans during pregnancy is unclear.

Animal Data
Lifitegrast administered daily by intravenous (IV) injection to rats, from pre-mating through gestation day 17, caused an increase in mean preimplantation loss and an increased incidence of several minor skeletal anomalies at 30 mg/kg /day, representing 3,400-fold the human plasma exposure at the RHOD of Xiidra, based on AUC. No teratogenicity was observed in the rat at 10 mg /kg /day (460-fold the human plasma exposure at the RHOD, based on AUC.). In the rabbit, an increased incidence of omphalocele was observed at the lowest dose tested, 3 mg /kg /day (400-fold the human plasma exposure at the RHOD, based on AUC), when administered by IV injection daily from gestation days 7 through 19. A fetal No Observed Adverse Effect Level (NOAEL) was not identified in the rabbit.

Lactation
There are no data on the presence of lifitegrast in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to lifitegrast from ocul ar administration is low. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for Xiidra and any potential adverse effects on the breastfed child from Xiidra.

Pediatric Use
Safety and efficacy in pediatric patients below the age of 17 years have not been established.

Geriatric Use
No overall differences in safety or effectiveness have been observed between elderly and younger adult patients.

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis: Animal studies have not been conducted to determine the carcinogenic potential of lifitegrast. Mutagenesis: Lifitegrast was not mutagenic in the in vitro Ames assay. Lifitegrast was not clastogenic in the in vivo mouse micronucleus assay. An in vitro chromosomal aberration assay using mammalian cells (Chinese hamster ovary cells), lifitegrast was positive at the highest concentration tested, without metabolic activation.

Impairment of fertility: Lifitegrast administered at intravenous (IV) doses of up to 30 mg/kg/day (5400-fold the human plasma exposure at the recommended human ophthalmic dose [RHOD] of lifitegrast ophthalmic solution, 5%) had no effect on fertility and reproductive performance in male and female treated rats.

Manufactured for: Shire US Inc., 300 Shire Way, Lexington, MA 02421. For more information, go to www.Xiidra.com or call 1-800-828-2088. Marks designated * and TM are owned by Shire or an affiliated company. ©2018 Shire US Inc. SHIRE and the Shire Logo are trademarks or registered trademarks of Shire Pharmaceutical Holdings Ireland Limited or its affiliates. Patented: please see https://www.shire.com/legal-notice/product-patents Last Modified: 01/2018 533769
Xiidra® is the only LFA-1 antagonist approved to treat the signs and symptoms of Dry Eye Disease (DED).1,3

Xiidra is designed to target the interaction between LFA-1 on T cells and ICAM-1. ICAM-1 may be overexpressed in corneal and conjunctival tissues in DED. This interaction is a key mediator of inflammation, which may contribute to the chronic and sometimes progressive nature of DED and perpetuate the signs and symptoms.1

In vitro studies have shown that Xiidra may inhibit the recruitment of previously activated T cells, the activation of newly recruited T cells, and the release of pro-inflammatory cytokines.1

The exact mechanism of action of Xiidra in DED is not known.1

For additional safety information, see accompanying Brief Summary of Safety Information on the adjacent page and Full Prescribing Information on Xiidra-ECP.com.


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