Glaucoma treatment options continue to undergo changes, with the introduction of new medications and with new glaucoma drug delivery options on the horizon. The recent publication of the LiGHT Study, evaluating selective laser trabeculoplasty (SLT) as a first-line treatment for glaucoma, gives optometrists more options than ever to consider for the treatment of their patients with glaucoma. In this article, I review glaucoma medications that have recently been introduced to the market and look ahead to some future glaucoma drug delivery options.

**THE PHARMACEUTICAL LANDSCAPE**

Prostaglandin analogues remain the initial treatment of choice for many ODs, with their once-daily use schedules and well-known efficacy in lowering IOP. Two products have been added to this class in recent years.

Latanoprostene bunod 0.024% (Vyzulta, Bausch + Lomb) received FDA approval in 2017. It is a prostaglandin analogue, specifically a nitric-oxide-donating prostanoid FP receptor agonist. The drug’s unique mechanism of action both increases uveoscleral outflow and relaxes the trabecular meshwork to improve conventional outflow. Like other prostaglandins, it is dosed once a day.

Two phase 3 noninferiority clinical trials, APOLLO and LUNAR, demonstrated significantly lower mean IOP with latanoprostene bunod compared to timolol at all time points. In those trials, baseline IOP was about 26 mm Hg in the latanoprostene bunod group, and by 3 months average diurnal IOP had dropped to 18.1 mm Hg. The medication was well tolerated, with conjunctival hyperemia occurring in 5.9% of patients.

Another prostaglandin analogue formulation, latanoprost ophthalmic emulsion 0.005% (Xelpros) was approved by the FDA in 2018. This is the first latanoprost product not...
formulated with the preservative benzalkonium chloride, although it does contain a preservative. In randomized clinical trials, the latanoprost emulsion was shown to reduce IOP in patients with open-angle glaucoma and ocular hypertension by a mean 6 mm Hg to 8 mm Hg.3,4

Recently a new drug class, rho-kinase inhibitor, has emerged as a treatment option for our glaucoma patients. The rho-kinase inhibitor netarsudil 0.02% (Rhopressa, Aerie Pharmaceuticals) was approved in 2017. A fixed combination of netarsudil 0.02% and latanoprost 0.005% (Rocklatan, Aerie Pharmaceuticals) was approved last year.

Netarsudil 0.02%, dosed once daily in the evening, lowers IOP by enhancing outflow through the trabecular meshwork and by reducing episcleral venous pressure.5 Two phase 3 clinical trials, ROCKET-1 and ROCKET-2, demonstrated that netarsudil once daily was noninferior to timolol twice daily in patients with baseline IOPs less than 25 mm Hg.6 The most common adverse event in those studies was conjunctival hyperemia, reported in 53% of patients.6 The demonstrated efficacy of this medication has shown it to be a useful adjunct agent for the treatment of glaucoma.

The fixed combination of netarsudil 0.02% and latanoprost 0.005%, also dosed once daily in the evening, lowers IOP by enhancing outflow through the trabecular meshwork, increasing uveoscleral outflow, and reducing episcleral venous pressure. Two trials, MERCURY-1 and MERCURY-2, compared netarsudil alone versus latanoprost alone versus netarsudil/latanoprost.7,8 In those trials, 62% of patients receiving netarsudil/latanoprost achieved >30% reduction in mean diurnal IOP at 3 months, compared with 33% in latanoprost-treated patients.7,8 The most common adverse event in those studies was conjunctival hyperemia, reported in 59% of patients.7,8

**GLAUCOMA DRUG DELIVERY**

The search for innovative ways to get glaucoma medications to target tissues has been under way for some time. The perceived benefits of drug delivery devices include reduced cost to patients, increased compliance, and fewer ocular side effects. Challenges include achieving efficacy over an extended delivery period and uncertainty regarding patient acceptance of the devices.

A study published in 2018 aimed to assess patients’ acceptance of six potential drug delivery approaches.10 For this study, 199 patients filled out a questionnaire, and investigators calculated their acceptance rates. The acceptance rates, in descending order, were as follows:

- triple combination eye drop, 85%
- microdose eye spray, 54%
- drug-eluting periocular ring insert, 43%
- injectable subconjunctival drug insert, 32%
- drug-eluting contact lens, 31%
- injectable anterior chamber implant, 30%

Patients who had more significant glaucoma or had undergone invasive glaucoma surgery were more likely to consider alternative options to traditional eye drops.10

The FDA recently cleared one new glaucoma drug delivery device and one more new devices in development may make it to the market in the near future.

**Microdose Latanoprost**

A microdose formulation of latanoprost (MicroProst, Eyenovia) is in development. This mode of delivery has the advantages of using 75% less drug and preservative than topical application and still getting 88% of the drug to the target tissue and achieving IOP lowering of 29%.11 Patients still need to administer the medication, so compliance concerns are greater with this approach than with other drug delivery devices that are placed inside the eye or on the eye in other ways. An ongoing phase 3 study is assessing microdose latanoprost in chronic angle-closure glaucoma, open-angle glaucoma, and ocular hypertension.

**Bimatoprost Ring**

The bimatoprost ring (Allergan), a topical ocular insert administered by a physician, is designed to release prostaglandin for up to 6 months per administration. The ring, made in multiple sizes, is a soft, flexible insert that rests circumferentially in the fornices on top of the conjunctiva.12 A phase 2 clinical trial in 130 patients compared a ring containing 13 mg of bimatoprost versus timolol maleate instilled twice daily.12 The ocular insert achieved IOP lowering of 4 mm Hg to 6 mm Hg with a retention rate of 89%. Patients assessed the ring’s comfort with a 90% acceptance rate at 6 months.12

**Punctal Plugs**

Optometrists use punctal plugs on a daily basis to manage ocular surface disease. Two intracanalicular drug inserts are undergoing clinical evaluation in the United States. OTX-TP (Ocular Therapeutix) is a resorbable intracanalicular insert that can deliver travoprost to the ocular surface for up to 90 days without preservatives. In a phase 3 clinical trial, the insert lowered IOP by between 3.27 mm Hg and 5.27 mm Hg in patients with primary open-angle glaucoma or ocular hypertension.

An L-shaped punctal plug with a latanoprost core (Evolute, Mati Therapeutics) is designed to create a unidirectional flow into the tear film to reduce systemic absorption of the drug. A phase 2 clinical trial showed a 20% reduction in IOP at 3 months with 92% retention.13

**Subconjunctival Implants**

A biodegradable implant that can be placed in the subconjunctival space at the slit lamp (Durasert, EyePoint Pharmaceuticals) is undergoing phase 1
and 2 clinical trials. The 3 mm by 0.3 mm implant releases latanoprost over a period of 12 months.

**Intracameral Implants**

In March the FDA approved the biodegradable bimatoprost sustained-release intracameral implant 10 mcg (Durysta, Allergan) for intracameral administration to treat open angle glaucoma or ocular hypertension. The implant is injected into the anterior chamber and typically resides in the inferior angle, where it elutes bimatoprost in a sustained manner.

**Contact Lenses**

Contact lenses that elute medication have been considered as a route to achieve long-term delivery of glaucoma drugs. Comfort, compliance with wearing the lenses, optical characteristics of the lens, ocular surface disease concerns, and replacement schedules are among the challenges that have been encountered in preclinical and clinical trials.

**Dioptrer Corp.** is studying an approved contact lens combined with a patented drug-eluting process and approved drugs to treat a variety of diseases, including glaucoma. The device uses vitamin E nano-barriers to extend drug release. In a small phase 1 clinical trial, patients received the drug-containing lens for a 2-day dosing period. A reduction of IOP was observed over 9 days after the lens was removed. A phase Ib study and phase 2 study are planned for the second and third quarter of 2020.

**MANY OPTIONS ON THE HORIZON**

It is an exciting time in the world of glaucoma management and treatment. New options continue to emerge that allow ODs to provide effective IOP lowering to slow the progression of glaucoma in their patients. In the near future, if the promise held by some of the drugs and devices described here continues to bear fruit, optometrists will be able to consider not only the selection of the most effective topical medications, but also the best drug delivery options to match the needs of their patients with glaucoma.