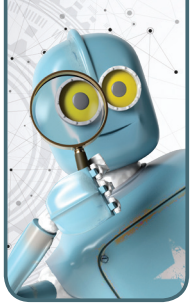


COMING SOON: PRESBYOPIA-CORRECTING EYE DROPS

They're on their way; here's what you need to know.

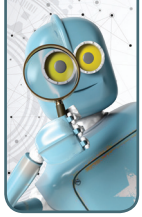
BY JOSHUA DAVIDSON, OD, FAAO, FSLS; AND PAUL KIMBRO, OD

Patients who have been emmetropic their whole lives and are now presbyopic represent an enormous market for the eye care community. By one projection, there will be more than 2 billion people with presbyopia worldwide this year.[1] These individuals are typically in their late 40s, 50s, and even well into their 60s, and are at the apex of their earning potential. They demand options and have learned not to accept anything less than the latest and greatest. Seeing this opportunity, numerous companies have ramped up their research and development in an attempt to capture these patients.

Until now, the only options available for these presbyopes have been wearing corrective lenses or undergoing an elective surgical procedure such as excimer laser ablation, multifocal or accommodating IOL implantation, corneal inlays, or femtosecond laser instrastromal correction. Now, however, the options for improving our patients' presbyopia appear to be poised for a large boost, as numerous companies are nearing regulatory approvals for presbyopia-correcting eye drops. These drops can be divided into two categories: miotic-based eye drops and lens restoration drops. Each has its own mechanism of action, which we discuss below.

MIOTIC-BASED EYE DROPS

This type of presbyopia drop functions by constricting the pupil, thereby inducing a pinhole effect and increasing the patient's natural depth of field. Miotics enhance near vision due to the greater depth of focus secondary to pupillary constriction. Years of research have resulted in drops that are now comfortable and tolerable upon instillation, are fast acting with sustained results, incur no substantial decrease in distance vision, and have an excellent safety profile that avoids traditional miotic problems such as headaches, decreased



contrast sensitivity, and decreased night vision. Numerous companies are pursuing this route.

Proprietary Presbyopia Drop

Allergan, an AbbVie Company, may likely be the first to market with an FDA-approved presbyopia-correcting drop. The company's investigational eye drop is currently in two identical phase 3 trials, GEMINI 1 and GEMINI 2, evaluating its safety and efficacy in study participants with presbyopia. Phase 2 studies are complete, with results scheduled to be presented at upcoming eye care congresses this year.

PRX-100

Much like the Allergan compounds, PRX-100 (Presbyopia Therapies) has been developed to induce a reversible pupil miosis that should improve near vision through increased depth of focus. This drop's active ingredient is aceclidine. According to the company, PRX-100 will have a 30-minute onset of action and will last approximately 4 hours. It is meant to be used binocularly. Interestingly, with PRX-100 there is no expected impact on accommodation, only miosis. Pilocarpine, which is the gold standard agent for miosis, also induces accommodation and has been found to decrease distance vision due to its action on the ciliary muscle and the pupillary sphincter muscle. It is also notorious for causing browache and conjunctival hyperemia. The company claims that its drop will affect only the pupillary sphincter muscle, sparing the ciliary muscle and having no effect on accommodation, thereby preserving stable distance vision. It is expected that this drop will enter FDA phase 3 clinical trials in 2020.

CSF-1

CSF-1 (Orasis Pharmaceuticals) is a parasympathomimetic agent combined with a nonsteroidal antiinflammatory drug in an oil-based vehicle that adds to the comfort of the drop. At this time, the company has not disclosed the ingredients of CSF-1, only stating that the drop contains a "proprietary combination of existing and well-studied ingredients." The oil-based vehicle has been found to reduce discomfort caused by ciliary spasms and to reduce the risk of uveitis. The active ingredient is a low-dose pupillary miotic, and the agent is to be administered binocularly. The company states that clinical studies have demonstrated significant improvements in near vision while maintaining a high safety profile. The improvement included a reported 3-line improvement in near vision with no substantial reduction in distance vision at both regular and low luminance. The company has reported a successful phase 2 study[2] and says it is "advancing towards phase 3 development."

EyeFocus

Eye Focus (OSRX Pharmaceuticals) is a binocular presbyopia-correcting drop that is a compounded combination of medications including pilocarpine, phenylephrine, pheniramine, and ketorolac. The company expects to release two different strengths, branded as EyeFocus and EyeFocus+, in the third quarter of 2020. (Because compounded medications are not subject to FDA approval, the release of these drops is not dependent on a regulatory timeline.) The drops work by constricting the pupil and improving accommodation at the ciliary body, with the difference between the two being the strength of pilocarpine HCl. EyeFocus contains 0.302% pilocarpine HCl and EyeFocus+ contains 0.604% pilocarpine HCl.

EyeFocus is expected to work by pilocarpine stimulating both accommodation and pupillary miosis, while phenylephrine, nepafenac, and pheniramine work to stop excess pupil constriction and counteract ciliary muscle spasm, vascular congestion, and the hyperemia induced by pilocarpine. Naphazoline functions by intensifying the relaxing effect of pilocarpine on the dilator pupillae. All of these synergistic effects improve near vision, preserve distance vision, and reduce side effects such as hyperemia and headaches.

In a small proof-of-concept study, nine presbyopic patients received one drop of the medication in each eye at hour 1 and then another drop at hour 5. In these patients, near vision improved by an average of 3 lines. At hour 1, 66% of patients could read at least 20/40. During hours 3 to 5, reading vision was 20/40 in 89% of patients and 20/30 in 66% to 71% of patients. Notably, 78% of patients maintained 20/40 vision for 8 hours [unpublished data].

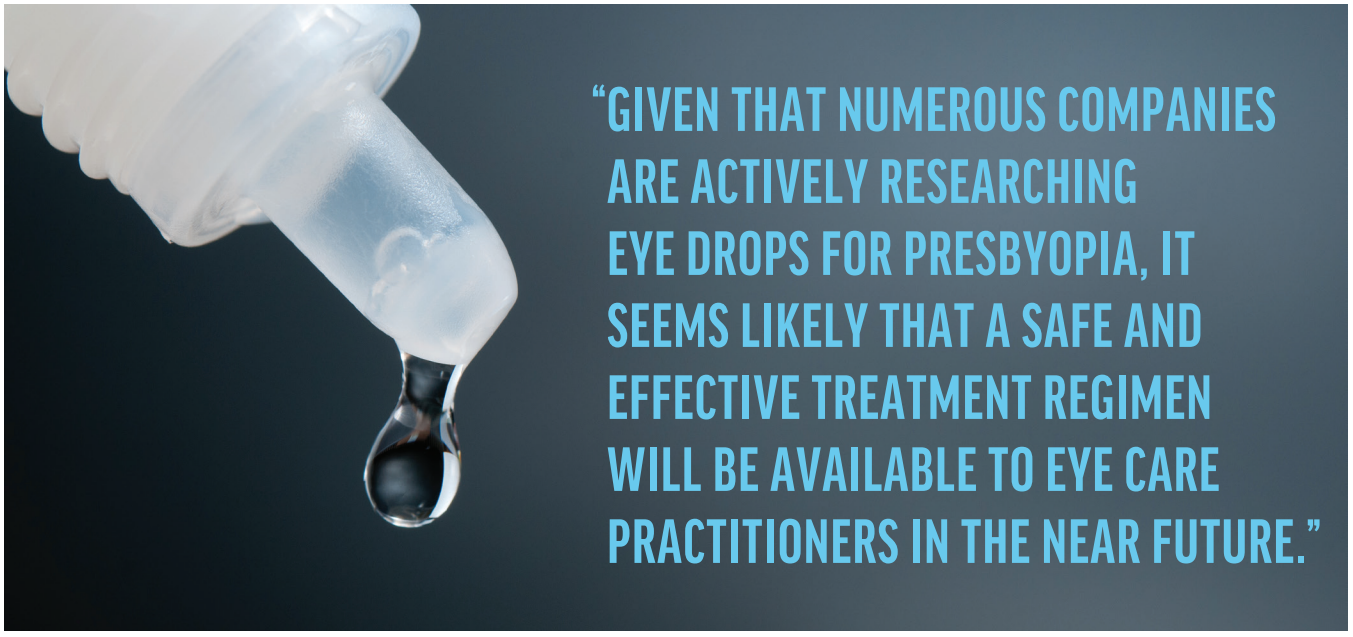
LENS RESTORATION DROPS

The second category of presbyopic eye drops seeks to revitalize a patient's aging crystalline lens. There is only one product known to be in development in this category.

UNR844-CI

UNR844-CI (Novartis) is a first-in-class, disease-modifying topical treatment for presbyopia that uses a potent antioxidant known as lipoic acid choline ester (1.5%) to break apart the disulfide bonds that form between proteins within the crystalline lens fiber cells, thereby increasing lens flexibility and restoring partial elasticity.

This prodrug is topically instilled binocularly, whereupon it penetrates the cornea and degrades into two naturally occurring substances, lipoic acid and choline. The lipoic acid is then hydrolyzed by esterase in the tear film into dihydrolipoic acid,



which destroys the disulfide bonds in the lens, improving flexibility as noted earlier. An interesting hypothesis regarding this medication is that it may potentially halt or even reverse the natural lens hardening that occurs with age, thereby allowing a potential restoration of natural accommodation.

In phase 1 and 2 studies, UNR844 exhibited a good safety profile and there were no treatment-related study discontinuations. In addition, all patients showed substantial near visual acuity improvements by day 15.[3,4] By day 91, 82% of patients had 20/40 or better near vision and 36% had 20/25 or better near vision. Novartis expects the drop to be labeled for use twice daily for approximately 90 days. The effects of this dosing regimen have been found to last up to 7 months without further dosing.[3,4] Novartis has said that it plans to file for marketing approval in 2021.

GET READY FOR THE FUTURE

Optometrists need to be ready to offer our patients the latest, greatest, and safest innovations in eye care. Given that numerous companies are actively researching eye drops for presbyopia, it seems likely that a safe and effective treatment regimen will be available to eye care practitioners in the near future. It is expected that these drops will be geared toward pre–cataract-age patients with presbyopia who have enjoyed great distance vision throughout their lives and those who have previously had refractive surgeries including LASIK, PRK, or SMILE.

With pupillary miotics likely to be the first pharmaceutical treatment for presbyopia to market, optometrists need to understand how they function and whom they are designed for. These treatments have shown benefit in numerous studies and appear poised to help many of our patients with presbyopia. In addition to improving patients' near vision, the topical miotics may also help address aberrations that are amplified by large pupil sizes, including those caused by previous refractive surgeries.

For many ODs, the potential financial benefit of an effective topical presbyopia drop cannot be overlooked, as we have seen continued erosion of contact lens and eyeglass sales due to online sellers. Pharmaceutical presbyopia management could provide an increased demand for our prescribing services and drive patients into our offices. In this time of great change, the influx of presbyopia eye drops hitting the market should be an event that all eye care practitioners look forward to. ■

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