THE SCOOP ON PHARMACEUTICAL PRESBYOPIA TREATMENT OPTIONS

Taking stock of current and future offerings to address this common condition.

BY MARK SCHAEFFER, OD

Optometrists have been treating presbyopia since the beginning of our existence as eye care professionals. We've seen technologies come a long way, from eyeglasses to contact lenses to surgical options, and now pharmaceutical interventions have entered the space (see *A Timeline of Treatment Options for Patients With Presbyopia*).

Because presbyopia affects 128 million Americans,[1] the condition brings a steady stream of patients into offices across the country. This year, 1.4 million people will become new presbyopes.[1] That's three people every minute!

For many patients, presbyopia is the reason for their first encounter with an optometry office or with a new optometrist. Regardless of what brings them to *our* chair, we educate all patients with presbyopia about every treatment option available and explain how they may or may not be suitable for them. Involving patients in the conversation and providing them with all their options gives them a say about what will work for their lifestyle.

Patients are excited about the ability to reduce their reliance on eyeglasses with the addition of a pharmaceutical treatment for presbyopia. Several options are rapidly progressing through clinical trials and FDA approval and will help shape how more patients will access this treatment.

FDA APPROVAL FOR A FIRST-IN-CLASS MEDICATION

Pilocarpine HCl ophthalmic solution 1.25% (Vuity, Allergan/AbbVie) was FDA-approved in October 2021,[2] and in April, it was granted twice daily dosing by the agency.[3] In the VIRGO trials evaluating this drop, patients were dosed twice daily: once at time zero and another dose 6 hours later.[4] In these trials, 37% of patients achieved a greater than 3-line gain in near visual acuity at day 14, hour 9. The data were further analyzed for a 2-line gain in visual acuity, which more than 60% of participants achieved at day 14 hour 9. The safety profile for twice daily drops showed minimal experience of any adverse events,

A TIMELINE OF TREATMENT OPTIONS FOR PATIENTS WITH PRESBYOPIA

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English monk and Scientist Roger Bacon writes about his experiments using convex lenses to correct vision, advocating their use to help "old people."[1]

1999

Focus Progressives (CIBA Vision, now a part of Alcon) aspheric soft contact lenses receive approval from the FDA for the optical correction of presbyopia.[2]

2004

NearVision CK (Refractec) is approved by the FDA as the first surgical procedure for the correction of presbyopia.[3]

2021

The FDA approves pilocarpine HCl ophthalmic solution 1.25% (Vuity, Allergan/AbbVie), the first eye drop to treat presbyopia.[4]

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2. Package insert for the Focus family of (vifilcon A) soft contact lenses. CIBA Vision. August 1999. Accessed August 10, 2023. www.optikkandr.com/wp-content/uploads/Ciba-Vision-Focus-Progressives-Vifilcon-A-Visitint.pdf
3. Rundle RL. Refractec gets FDA approval for its presbyopia treatment. *The Wall Street Journal*. March 22, 2004. Accessed August 11, 2023. www.wsj.com/articles/SB107991800502561479
4. US Food and Drug Administration approves VUITY (pilocarpine HCl ophthalmic solution) 1.25%, the first and only eye drop to treat presbyopia (age-related blurry near vision) [press release]. AbbVie. October 29, 2021. Accessed August 11, 2023. https://news.abbvie.com/news/press-releases/us-food-and-drug-administration-approves-vuity-pilocarpine-hci-ophthalmic-solution-125-first-and-only-eye-drop-to-treat-presbyopia-age-related-blurry-near-vision.htm

with 9% of patients reporting a headache. In both once and twice daily drops, efficacy showed the greatest improvement by day 14, which confirms the neuroadaptation process we see with progressive ADD lenses and multifocal contact lenses.

AWAITING FDA APPROVAL

Pilocarpine 0.4% (CSF-01, Orasis Pharmaceuticals) is under FDA review for approval with a PDUFA date of October 22, 2023. This formulation of low-dose pilocarpine is dosed up to twice daily, with the second drop dosed at around 2 to 3 hours after the first drop to extend its duration to 8 hours. The drop is preservative-free, with a near-neutral pH and contains various lubricating agents in the vehicle. It is packaged in single-use vials.

In FDA trials, NEAR-1 and NEAR-2, key primary and secondary endpoints were reached: 40% of participants demonstrated a 3-line gain 1 hour post-dose one, and 50% demonstrated a 3-line gain 1 hour post-dose two.[5] Other data from the study showed that 86% of participants achieved 20/40 or better binocular near vision at 1 hour post-dose two.[5]

IN THE PIPELINE

Four companies are currently in FDA trials with investigational products. Below, I discuss what differentiates each product, how they compare to current treatments, and what to look for in the future.

Carbachol 2.75% + brimonidine 0.1%

Carbachol 2.75% + brimonidine 0.1% (Brimochol PF, Visus Therapeutics) is a miotic, cholinergic agonist that binds and activates acetylcholine receptors. It has been used to treat glaucoma by increasing aqueous outflow. The once-daily drop is a fixed combination with carbachol used to produce durable miosis and brimonidine to increase bioavailability of carbachol, inhibit pupil dilation, and reduce ocular hyperemia. In the company's clinical trial, BRIO-1, the molecules were tested together in combination and individually. The molecules together were significantly superior at pupil diameter reduction up to 10 hours post-administration. At peak effect, 50% of respondents had > 15 EDTRS letter gain without a > 5 EDTRS letter loss at distance.[6] In Snellen equivalent, up to 84% of patients achieved a VA of 20/40 or better at max effect and > 50% experienced this effect even at 8 hours post-administration.[6]

Aceclidine 1.75%

Aceclidine 1.75% (LNZ-100, Lenz Therapeutics) and aceclidine 1.75% + brimonidine (LNZ-101, Lenz Therapeutics) are pupil-selective miotics designed to target the iris sphincter muscle with less effect on the ciliary muscle. This mechanism of action creates a lower corresponding myopic shift in patients while still producing a miotic pupil. Aceclidine has been approved for the treatment of glaucoma in the European Union since the 1970s with 400 million doses prescribed and approved at higher doses.

The phase 2 INSIGHT study examined aceclidine 1.75% and aceclidine 1.75% + brimonidine over a 10-hour time span. The doses of aceclidine alone showed a higher response rate initially, while the aceclidine 1.75% + brimonidine showed the higher response rate in the later time points (after 9 hours).[7] As shown with carbachol + brimonidine, the addition of brimonidine seems to help increase the bioavailability of aceclidine, which simulates an extended release into later hours.

Phentolamine

The preservative-free ophthalmic solution containing 0.75% phentolamine or 1% phentolamine mesylate (Nyxol, Ocuphire Pharma) is a nonselective alpha-1 antagonist that targets the iris dilator muscle to

inhibit dilation. This creates a miotic pupil without affecting the ciliary muscles. It is the only miotic that is not a cholinergic agent.

If this drug sounds new and familiar at the same time, that's because it is awaiting FDA approval for the reversal of mydriasis with a PDUFA date of September 28. In its presbyopia phase 2 trial, VEGA-1, four arms were created with: Nyxol alone, Nyxol + low-dose pilocarpine 0.4% (LDP), LDP alone, and placebo alone.[8] In the Nyxol alone group, 30% of patients gained > 15 letters at hour 12 post-administration, and 53% gained > 10 letters. At hour 12, 56% of patients had achieved 20/40 or better Snellen equivalent. When adding LDP, rapid onset of efficacy is seen, with 61% of patients having a 15-letter gain at 30 minutes post-administration.

Pilocarpine 2%

Pilocarpine 2% (MicroLine, Eyenovia) is a cholinergic miotic that is delivered using the company's proprietary Optejet dispenser and pilocarpine with micro-array print formulation. The spray releases one-fifth the amount of a drop to increase bioavailability and reduce exposure to preservatives. Eyenovia's FDA phase 3 trial, VISION-2, met the endpoint of a statistically significant proportion of patients showing a 15-letter gain at near without a 5-letter decrease at distance at 2 hours in low light conditions.[9]

INFORMED PROVIDERS OFFER BETTER CARE

We say this about many areas of eye care, but it's an exciting time to be a practitioner treating presbyopia.

> FOR MANY PATIENTS, PRESBYOPIA IS THE REASON FOR THEIR FIRST ENCOUNTER WITH AN OPTOMETRY OFFICE OR WITH A NEW OPTOMETRIST.

We have more options in glasses and contact lenses, and even the pharmaceutical options are growing quickly. By understanding the nuances of the drops that are available and by being able to incorporate those that appear on the horizon, we can provide better care for our patients and help them understand the frustrating and ubiquitous condition that is presbyopia. ■

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