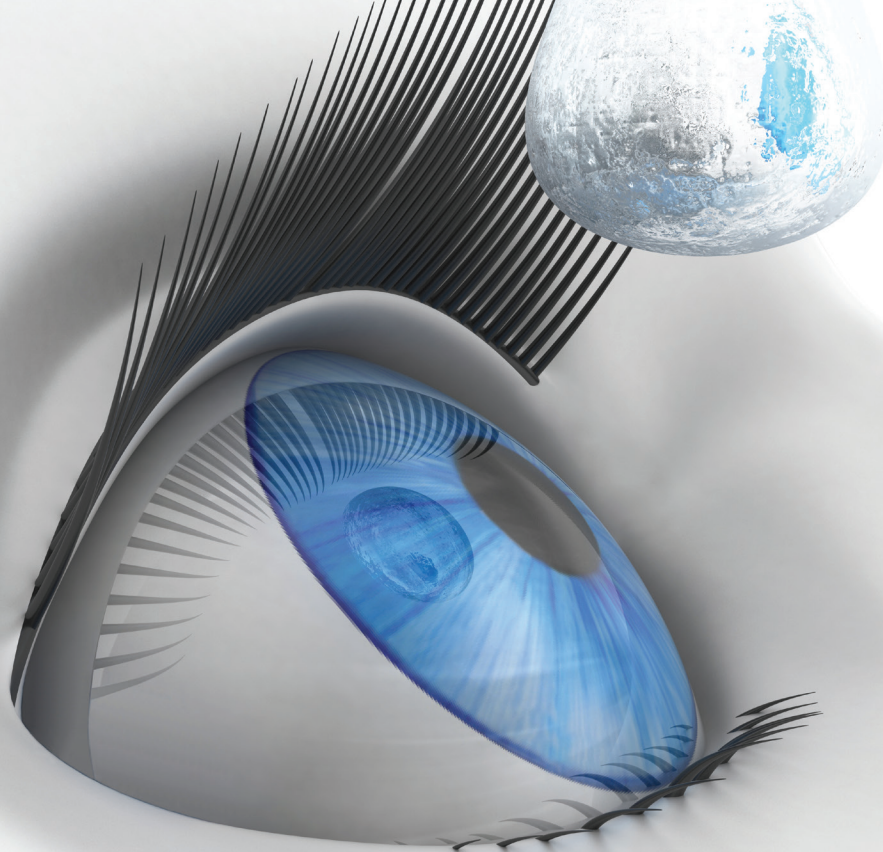
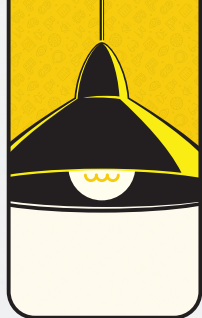




THE LATEST ROUNDUP OF KEY PRESBYOPIA-CORRECTING DROPS



Watch out for updates on drops in development.

BY SELINA R. MCGEE, OD, FAAO, DIPL ABO

Approximately 128 million people in the United States have presbyopia, and with millennials beginning to turn 40 this year, that number is bound to increase.¹ Add this group of 73 million millennials to the 61 million Generation Xers,² many of whom are in their 50s, and you find that presbyopia eclipses any other refractive

error or disease that we treat in terms of affected population size. Imagine the influx of patients when they start calling to schedule appointments for prescription presbyopia drops. To make sure we're properly prepared to educate and treat our patients about the newest presbyopia treatment modality, let's review what's available and what's in the pipeline (Table).

FDA-APPROVED

Pilocarpine HCl ophthalmic solution 1.25% (Vuity, Allergan, an AbbVie company) was the first-in-class eye drop to treat presbyopia, receiving FDA approval in October.³ Vuity is an optimized formulation of pilocarpine delivered with Allergan's proprietary pHast technology vehicle, which allows the drop to adjust to the physiological pH of the tear film.³ Approval was based on data from the phase 3 GEMINI 1 and GEMINI 2 clinical studies. In both studies, Vuity met the primary endpoint, reaching statistical significance in improvement of near vision in low light conditions without a loss of distance vision compared with the vehicle on day 30 at hour 3.³ The most common adverse events, occurring at a frequency of > 5%, were headache and eye redness; there were no serious adverse events.³

IN THE PIPELINE

Two proprietary pupil-modulating eye drop combinations of carbachol and brimonidine tartrate, **Brimochol** and **Brimochol-F** (Visus Therapeutics), have been studied in six clinical studies evaluating their safety and efficacy in restoring near vision loss associated with presbyopia. In the most recent study of 85 patients, in

**TABLE.** Approval Status of Presbyopia-Correcting Drops*

DROP	COMPANY	MOA	APPROVAL STATUS
Brimochol, Brimochol-F	Visus Therapeutics	Miotic	Phase 3 trials planned
CSF-1	Orasis Pharmaceuticals	Miotic	Phase 3
Dioplin	Novartis	Lens softening	Phase 2
LNZ100, LNZ101	Lenz Therapeutics	Miotic	Preparing for phase 3
MicroLine	Eyenovia	Miotic	First phase 3 complete
Nyxol + low-dose pilocarpine	Ocuphore Pharma	Miotic	Phase 2 enrollment completed
Vuity	Allergan	Miotic	FDA approved

Abbreviation: MOA, mechanism of action

*Not an exhaustive list.

the per protocol population, a minimum of 83% of participants treated with Brimochol, Brimochol F, or carbachol monotherapy (Carbachol F, the active comparator drug) achieved 3 lines of improvement in binocular near visual acuity under mesopic conditions at 1 hour without losing 1 line of distance vision. A minimum of 82%, 52%, and 35% of participants met this same endpoint at 3, 7, and 9 hours, respectively.⁴ The company plans to begin phase 3 trials soon.

CSF-1 (Orasis Pharmaceuticals) is a preservative-free solution that contains a proprietary combination of low-dose pilocarpine and a multifaceted vehicle.⁵ After seeing promising results from its phase 2b study, and receiving Series C funding, the company has initiated multi-center, double-masked, parallel-group phase 3 studies,⁶ NEAR-1 and NEAR-2.^{7,8}

UNR844-CI (Dioplin, Novartis) is a prodrug that penetrates the cornea and uses lipoic acid choline ester to reduce disulfide bonds in the lens, which, over time, may restrict the lens from changing shape via ciliary muscle contraction and relaxation. The age-related disulfide bonds also contribute to the development of nuclear sclerotic cataracts. A phase 2 study showed that 82% of participants had 20/40 or

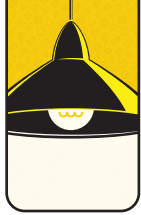
better visual acuity and 36% had 20/25 or better visual acuity after 3 months.⁹

Aceclidine 1.75% (LNZ100, Lenz Therapeutics) and aceclidine 1.75% + brimonidine (LNZ101) use the same novel active ingredient to target the iris sphincter muscle to reduce pupil diameter, allowing more focused near vision.¹⁰ Aceclidine has also demonstrated the ability to stimulate the pupil with minimal effect on the ciliary muscle, thus avoiding myopic shift.¹⁰ In phase 2b, aceclidine was well tolerated and met primary endpoints for fast onset (81% gained at least 2 lines and 53% gained 3 lines in 30 minutes) and long duration (50% maintained 2-line improvement and 22% maintained 3-line for 7 hours).¹⁰ The company is currently preparing for a phase 3 trial later this year.

MicroLine (Eyenovia) is a proprietary pilocarpine formulation and candidate for the episodic treatment of presbyopia. The company's Optejet dispenser can deliver a small (7 µL) dose of pilocarpine that adheres uniformly to the ocular surface with an effect that lasts 3 to 4 hours.¹¹ The company announced positive results from the first phase 3 VISION-1 trial in May last year, which showed that the drop was significantly superior to a placebo at improving high contrast bin-

ocular distance corrected near visual acuity in low light conditions 2 hours after treatment.¹² The company announced in November that the second phase 3 VISION-2 trial involving 140 participants with presbyopia is currently enrolling and top-line data is anticipated mid-2022.¹²

Nyxol (Ocuphore Pharma) combines phentolamine ophthalmic solution 0.75% and low-dose 0.4% pilocarpine (LDP). VEGA-1 is a phase 2 multicenter, randomized, placebo-controlled, double-masked clinical trial evaluating a treatment combination of Nyxol, 0.75% phentolamine ophthalmic solution, and LDP.¹³ Ocuphore reported positive data from the VEGA-1 trial of this treatment combination mid last year. The study enrolled 150 patients at 17 investigational sites in the United States. On the primary endpoint, 61% of patients treated with Nyxol plus LDP improved 15 letters or more (≥ 3 lines) in photopic binocular near vision at 1 hour compared with 28% of patients who received a placebo (33% placebo adjusted difference; $P = .003$).¹³ Treatment with Nyxol and/or LDP alone did not reduce distance BCVA. Moreover, Nyxol and/or LDP was well tolerated with no headaches and had an effect for up to 6 hours.¹³



SET YOURSELF UP FOR SUCCESS

Keep an open mind and choose your patients wisely until you gain more clinical experience with the drop. I wanted to gain experience quickly with Vuity, so I set up a presbyopia consult day. I have been talking to my patients for the past year about a drop for presbyopia, and when it became available, I began reaching out to them. After compiling a list of potential candidates, I reached out to about 12 patients to come in and have the drop administered in the office. I chose a few emmetropic patients and a few distance-corrected contact lens patients (hyperopic and myopic). I took an administrative day to speak with these patients about their frustrations and expectations. I documented their current vision at near and ensured their excellent retina health. After waiting 15 minutes, we measured near vision and had patients look at their phones for a real-world experience. I sent them home with a short questionnaire about their experience and had them simply text their responses back to me. I then prescribed the drop electronically. My early clinic success has largely come from treating emmetropic patients and those who currently only wear distance correction who have mild to moderate presbyopia.¹⁵

With clinical experience, I have made changes to my protocol for presbyopia. For my patients whom I have seen in the last 6 months and who have a healthy retina, I am quite comfortable writing the prescription and having these patients use their drops at home. New patients will, of course, have a comprehensive exam with me first to ascertain if they are a candidate for presbyopia drops. Moving forward, follow-up appointments will either be done in the office or by telehealth appointment, or may become as simple as a check-in text, as our office does with spectacle and contact lens wearers.

I generally bill these services based on chief complaint and diagnosis, just as I would for any other disease state or visual condition. My advice is to make

QUESTIONS TO DRIVE YOUR CLINICAL PROTOCOL

If you're interested in offering presbyopia-correcting drops to your patients, the questions below can be helpful in determining candidates, ensuring positive outcomes, and getting you to think about your fees.

- Has this patient had a full comprehensive examination in the past 6 to 12 months?
- Is the patient's retina healthy?
- Is his or her prescription > -6.00 D?
- Does he or she have mild, moderate, or advanced presbyopia?
- What are his or her specific expectations and vision goals?
- How will I charge for my services?
- How can I leverage advances in presbyopia to market my practice?

the experience as frictionless as possible for the patient and charge for your expertise. I encourage doctors to prioritize their long-term relationships with patients, rather than the short-term financial gain, and to adjust their own approach as needed. For some tips on offering presbyopia drops, see *Questions to Drive Your Clinical Protocol*.

THE PRESBYOPIA OPPORTUNITY

We will finally be able treat new patients with presbyopia and minimal distance refractive error. Even our existing patients would love to have the option to try one or more of these products. Personally, I can't wait to see where the presbyopia revolution takes us. ■

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