A Look at a New Presbyopia Treatment

Presbyopia is a daily annoyance for many people over age 45, so it's no wonder that there's been considerable patient interest in—and buzz on social media about—the new eyedrop Vuity (pilocarpine hydrochloride ophthalmic solution, 1.25%; Allergan, an AbbVie Company).

The drug's FDA approval last October made it the first to market of the many presbyopia medications that are now in the pipeline (see next page). As additional approaches become commercially available, treatment for presbyopia is likely to be a moving target, with many new options for ophthalmologists and their patients to choose from. For now, though, Vuity is the only drop with a track record about which ophthalmologists can share their experiences and observations of efficacy and safety.

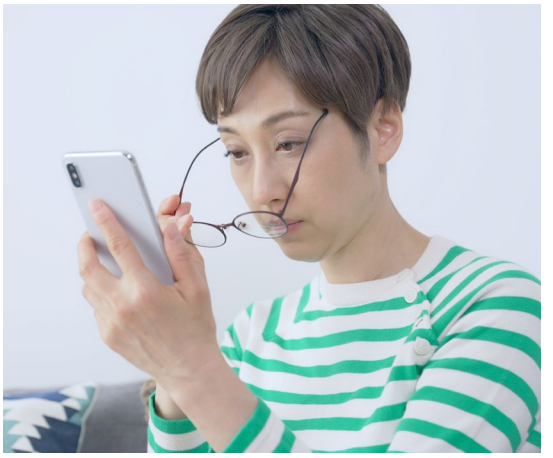
Efficacy and Patient Selection

Patient selection is key for getting good results, said Jeff Pettey, MD, MBA, at the University of Utah in Salt Lake City.

Task-specific vision. Patients who have the best results with Vuity are those who are highly motivated to function without reading glasses, said Linda Tsai, MD, FACS, at Washington University School of Medicine in St. Louis, Missouri. "They do better when they have a specific task in mind that they would like to do without glasses, like reading their cell phone or perhaps using the computer."

Accommodative reserve. Patients who still have some accommodative reserve are also good candidates for successful use of Vuity, said Dr. Pettey. "In general, patients who are early in their presbyopia or have a small myopic correction (–.25 D or –.50 D) have better results with Vuity."

Emmetropes. People who have had excellent vision all their lives tend to be frustrated with reading glasses, and they might be especially motivated to use drops. Dr. Pettey noted that one patient of his, a 47-year-old administrative assistant, grew weary of putting readers on and off for work. "She started Vuity and hasn't pulled out her glasses since starting the drop. She's delighted with the results," he said.



PRESBYOPIA. *Patients who are tired of readers may be candidates for presbyopia drops.*

Exam and Considerations

Martin L. Fishman, MD, MPA, in practice in Los Gatos, California, said he would advise prescribing Vuity only after doing a complete eye exam and an OCT scan of the macula.

Retinal complications. Dr. Fishman, also at Stanford University, pointed out that pilocarpine contracts the ciliary body, which may pull on the retina and lead to traction or tearing.

In several reported cases, patients who took pilocarpine 1.25% for presbyopia experienced retinal detachment or vitreofoveal traction.[1-3] And the Academy recommended in *Academy Express* that ophthalmologists report adverse events such as retinal tear or detachment to the FDA.[4]

Dr. Tsai added that she would be cautious with prescribing this drop to patients who have a history of high myopia because these patients are already at increased risk for retinal detachment.

She added that it's important to talk with patients about seeking attention if they experience new floaters or flashes or vision loss.

Other relative contraindications. Dr. Pettey advises using caution when considering Vuity in patients with risk factors for iridocyclitis and uveitis because pilocarpine can promote inflammation. Also, the Vuity prescribing information advises against iritis patients using the

BY KATHRYN MCKENZIE, CONTRIBUTING WRITER, INTERVIEWING **MARTIN L. FISHMAN, MD, MPA, JEFF PETTEY, MD, MBA,** AND **LINDA TSAI, MD, FACS.**

drug because iris-lens synechiae may form.

For patients with narrow angles, Dr. Fishman would hesitate to recommend the drug because pilocarpine has been known to shift the lens-iris diaphragm anteriorly and narrow the angle.

Additional advice. Finally, Dr. Tsai said, "patients with high expectations may not fare well with the medication."

Patient Education: Side Effects

For most patients, though, side effects are mild.

Headache and brow ache. In the GEMINI 1 phase 3 clinical trials for Vuity, headache was the most common side effect, occurring in 14.1% of study subjects, with 87% of those headaches considered brief and transient.[5]

"Headache can be severe enough to stop people from using the drop," said Dr. Pettey. "It seems to become less severe after the first week but remains in some." It is also reasonable to assume that patients who are prone to headache or eye pain are more likely to experience headache with the drop, he said.

"I make sure to warn patients about the brow ache in the beginning, because otherwise they are concerned when they get it," said Dr. Tsai. She noted, though, that the recommendation is for patients to use the drops for a week or longer, to see if side effects decrease. "I have not found pain relievers, such as Tylenol, to be very helpful in this instance and do not regularly recommend them."

Impaired vision. Also vital, said Dr. Fishman, is to inform patients that they need to exercise caution in darkness or dim lighting conditions because Vuity makes it difficult for the pupil to dilate. Dr. Tsai added that some of her patients have reported decreased peripheral vision and some dimming of their vision while they are using the drops. And the Vuity prescribing information advises patients against driving or operating machinery if they are experiencing blurred vision, which can result from accommodative spasm when patients switch from near to distance focus. Dr. Fishman added that in some countries, such as France, it is illegal to drive at night while using pilocarpine.

Red eye and irritation. Dr. Pettey said that after headache, red eyes and eye irritation are the most common side effects of Vuity, occurring in just a few of his patients.

In her practice, Dr. Tsai said that the patients who have experienced red eyes with instillation report that it subsides fairly quickly. Conversely, when it comes to eye irritation, she has had some patients who have "become more aware of surface irritation with the drop when

Miotic Presbyopia Treatments in the Pipeline

Vuity is the first of the miotic presbyopia treatments to come to market, but more are in the pharmaceutical pipeline.

Brimochol PF (Visus Therapeutics). Visus launched phase 3 clinical trials, BRIO-I and BRIO-II, in March 2022 for Brimochol PF. The double-masked, randomized, multicenter studies are expected to enroll 670 subjects who are either emmetropic phakic or pseudophakic presbyopic. The company reported encouraging results from its phase 2 trials for this drop, which combines the miotic agent carbachol and the alpha-2 agonist brimonidine tartrate.[1]

CSF-1 (Orasis Pharmaceuticals). Orasis announced the completion of the NEAR-1 and NEAR-2 phase 3 clinical trials last March for its low-dose pilocarpine drop. Promising data from the phase 2b trials were presented at the 2022 American Society of Cataract and Refractive Surgery annual meeting last April.[2] The phase 3 multicenter, double-masked, parallel-group trials enrolled more than 600 candidates in the United States.[3]

LNZ100 and LNZ101 (Lenz Therapeutics). The company is using a novel active ingredient in two formulations: aceclidine 1.75% and aceclidine with brimonidine. According to the company, this miotic targets the iris sphincter without overstimulating the ciliary muscle and thus does not impact distance vision.[4] At time of press, a phase 2, double-masked, multicenter study was underway with an expected study completion date in late 2022.[5]

MicroLine (Eyenovia). This 2% pilocarpine-based drug is delivered through a proprietary micromist dispenser, which may curb overdosing and waste associated with drops. Results were released in 2021 from a phase 3 trial for safety and efficacy,[6] and a second phase 3 trial was announced.

Nyxol (Ocuphire Pharma). Ocuphire combines Nyxol (phentolamine ophthalmic solution .75%) and low-dose .4% pilocarpine to inhibit iris muscle contraction in its presbyopia drop. The company reported positive data in 2021 of Nyxol in combination with low-dose pilocarpine—and of Nyxol alone in 2022.[7]

1 www.visustx.com/.
2 www.orasis-pharma.com/orasis-pharmaceuticals-to-present-new-data-on-novel-presbyopia-candidate-at-the-2022-american-society-of-cataract-and-refractive-surgery-ascrs-annual-meeting/.
3 www.orasis-pharma.com/orasis-pharmaceuticals-concludes-phase-3-clinical-trials-for-presbyopia-candidate/.
4 https://lenz-tx.com/pipeline/aceclidine.
5 https://clinicaltrials.gov/ct2/show/NCT05431543.
6 https://ir.eyenovia.com/news-releases/news-release-details/eyenovia-highlights-recent-progress-three-phase-3-programs-nda.
7 www.ocuphire.com/product-pipeline/nyxol.
All accessed Nov. 11, 2022.

using it for longer periods of time."

Other side effects. Other reported side effects mentioned in the GEMINI 1 study include increased tear production and nausea.[5] Dr. Tsai added that she had a patient who was told that her pupils looked small, and the patient was concerned about looking like she was under the influence of medications or drugs.

Additional advice. According to the Vuity prescribing information, contact lens wearers should remove their contacts to instill the drops and wait at least 10 minutes before reinserting contacts. And patients who use other eyedrops are advised to wait 5 minutes between Vuity and the other drop.

Usage in the Real World

In studies, about 30% of patients experienced a 3-line improvement in a mesopic, high-contrast environment compared to 8% with placebo.[5]

Mixed results. In the real world, results among patients have varied from no improvement to a significant improvement in near function.[6] For a number of patients, the effect of Vuity can be underwhelming, said Dr. Tsai. "Unless they are checking the reading chart provided in the Vuity box to document how much near vision is improved, patients may not get the sensation that they are improved much with the medication." However, she noted, according to the chart provided by Vuity, most patients are able to improve from 2 to 3 lines on the near chart. "For example, if they start at 20/30 at near, they might be able to get to 20/20."

Usage and duration. The recommended dosage is one drop per eye each day. The effect lasts five to six hours, with the most pronounced effect in the first three hours, according to the GEMINI 1 studies. Onset of effect is quick, said Dr. Tsai. "There is improvement noted in 10 to 15 minutes." She has had patients who work at the computer all day and find it useful, but she said, "Six hours is not long enough for most people." Because the effect is shorter than a traditional workday, Dr. Tsai thinks that occasional redosing in the short term would likely be fine; however, she noted that it is not yet FDA approved for use more than once daily.

Dr. Pettey said, "I've not recommended patients use the drop more than once daily given we are still early in our experience with it." However, he said he suspects that patients who have good results may be using it more than once a day.

What about cost? Vuity is not covered by insurance, so patients must pay out of pocket for it, approximately $80 per month. How this cost sits with patients can vary. "Cost can be a significant worry for some, while others would be willing to pay far more for any improvement," said Dr. Pettey.

For eligible patients, the company offers a program called MyVuityPoints (myvuitypoints.com), which allows patients to earn points toward discounts on future purchases or a free bottle.

Dr. Tsai said that most of her patients who inquire about the drops are "more than willing to pay that price." However, she added, "most are finding that the effectiveness of the drop doesn't justify the ocular discomfort and cost. Many tell me they stopped because it wasn't worth taking every day. They might keep it around to use for the right occasion, but otherwise they are just as happy using their reading glasses."

Long-term use. Although pilocarpine has been used for decades in glaucoma patients, the long-term effects of this new formulation remain to be seen.

Dr. Pettey said that he expects some of the effect of Vuity to wane for patients over time as each individual's accommodative reserve continues to diminish. "For those who continue to see benefit, I'm interested in any long-term effects to the ocular surface, although there are still patients on full-strength pilocarpine from the '80s going strong."

Dr. Tsai added, "I still remember the patients who previously used pilocarpine for glaucoma and ended up with miotic pupils or posterior synechiae, so I do have some concern that might occur again with patient use over many years."

Going forward. Although questions about Vuity remain, and there will be much to learn about the treatments due to be approved in the near future, Dr. Tsai noted that this is an area that should see much growth in the coming years.

1 Al-Khersan H et al. *Am J Ophthalmol.* 2022;242:52-55.

2 Amarikwa L et al. *Ophthalmic Surg Lasers Imaging Retina.* 2022;53(7):410-411.

3 Eton EA et al. *Retina Cases Brief Rep.* Published online Aug. 12, 2022. doi: 10.1097/ICB.0000000000001309.

4 www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home. Accessed Nov. 11, 2022.

5 Waring GO et al. *JAMA Ophthalmol.* 2022;140(4):363-371.

6 www.webmd.com/drugs/drugreview-182672-vuity-ophthalmic-eye. Accessed Nov. 11, 2022.

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