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# NOT JUST ANOTHER PILOCARPINE

An in-depth look at the new Qlosi™ topical drop for presbyopia.

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## INTRODUCTION

*As the presbyopic population continues to expand, eye care practitioners would like to have flexible, nonsurgical treatment options to offer these patients. Recently, new miotic eyedrops have emerged to fill the gap between spectacles and surgery. In the roundtable discussion featured here, two optometrists and an ophthalmologist discuss the newest-to-market miotic presbyopia drop, Qlosi™ (pilocarpine hydrochloride ophthalmic solution) 0.4% (Orasis Pharmaceuticals Inc.), which is now available to prescribe through BlinkRx or Medvantx pharmacies.*

**Ben Gaddie, OD, FAAO:** I'm joined here by two friends and experts in our field, Marjan Farid, MD, and Jessilin Quint, OD, MS, MBA, FAAO, to discuss pharmaceutical treatment options within the current presbyopia landscape. We'll review learnings from a previous launch in this space, and we'll discuss the new drug to market, Qlosi™ (pilocarpine hydrochloride ophthalmic solution) 0.4% (Orasis Pharmaceuticals Inc.). There were key learnings from the NEAR-1 and NEAR-2 pivotal clinical trials for Qlosi™, and we'll talk about how we eye care providers (ECPs) should translate those learnings clinically for our patients and how we can best set their expectations for using Qlosi™.

## THE CURRENT LANDSCAPE OF PRESBYOPIA TREATMENTS

**Dr. Gaddie:** According to the American Optometric Association, approximately 128 million Americans are presbyopes.[1] These individuals' eyecare needs are changing, and they want and need treatment options. Dr. Farid, let's start by discussing the current landscape of presbyopia

treatments. How have treatment options evolved, including surgical solutions, within the continuum of care in your practice?

**Marjan Farid, MD:** Until recently, we clinicians haven't had any pharmaceutical strategies to address presbyopia; we've managed it through surgical interventions such as LASIK and clear lens extraction/IOL implantation strategies. Yet, neither LASIK nor IOLs truly address the underlying issue of weakened accommodation in presbyopic eyes. Moreover, many presbyopes aren't interested in a surgical solution. In fact, most patients would welcome and benefit from the flexibility of a presbyopia eye drop that can be used either once per day or twice per day, depending on their near-range vision goals, to manage their presbyopia when they require it. With some recent pharmacological innovations, we're finally seeing nonsurgical, noninvasive treatments for presbyopia evolve and expand. It's an exciting time.

**Dr. Gaddie:** Dr. Quint, please describe the emergence of presbyopia treatments that include optical and contact-lens solutions that we optometrists use in clinical practice, as well as the pharmacological options that we've had in the past and their impact on our management of presbyopia.

**Jessilin Quint, OD, MS, MBA, FAAO:** For nonsurgical options, we had a presbyopic eye drop that worked by improving near vision by adjusting the pupil's size, sort of like a pinhole effect. Device-wise, we've seen recent innovations in multifocal contact lenses and progressive lenses. But, as you already stated, there is no shortage of presbyopic patients who are looking for flexible, noninvasive solutions to help them see better up close.

## QLOSI™: INTRODUCTION, FORMULATION, AND MECHANISM OF ACTION

**Dr. Gaddie:** We now have Qlosi™ (pilocarpine hydrochloride ophthalmic solution) 0.4%, which received FDA approval for the treatment of presbyopia in adults in October 2023. The Qlosi drop has a unique formulation and mechanism of action. Dr. Quint, please describe its formulation and your impression of its mechanism of action, as well as some of the features of Qlosi™.

**Dr. Quint:** Qlosi™ gives patients better focus for near objects without compromising their distance vision. Qlosi's EyeQ Formulation™ contains the lowest effective concentration of pilocarpine (0.4%) currently available, approximately one-third or less of the concentration of other formulations of pilocarpine drops. Qlosi™ has a near-neutral pH to increase its bioavailability, it is preservative-free, and it has two lubricating agents, HA and HPMC (Figure 1).

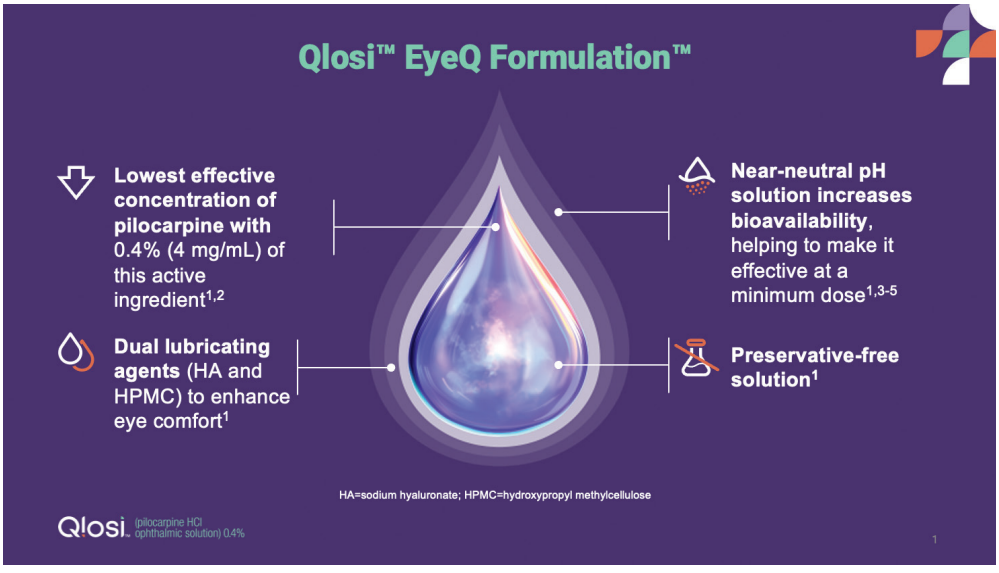


Figure 1. Qlosi™ EyeQ Formulation™ is the only FDA-approved eye drop with the lowest concentration of pilocarpine for optimal results.[1-3] Qlosi™ was able to reduce the concentration of pilocarpine and achieve pH levels that were near-neutral, thus increasing the bioavailability to make it effective at a minimum dose.[4,5] The preservative-free solution also has two lubricating agents to enhance eye comfort.[1]

1. Qlosi PI. Orasis Pharmaceuticals. 2024. 2. Vuity PI. AbbVie 2023. 3. Lenz Therapeutics Corporate Presentation. November 2024. 4. Anderson RA. *Brit J Ophthalmol.* 1968;52:607–611. 5. Mitra AK, Mikkelson TJ. *J Pharm Sci.* 1988;77(9):771–775. 6. Xu R, et al. *Optom Vis Sci.* 2016;93(11):1409–1419.

## NEAR-1, NEAR-2 CLINICAL TRIALS

**Dr. Gaddie:** The phase 3 pivotal trials for the approval of Qlosi™ (CSF-1) were named the NEAR-1 and NEAR-2 clinical trials[2]; I'll summarize some of their significant findings that could impact our clinical management of presbyopia.

NEAR-1 and NEAR-2 were two phase 3 multicenter, randomized, double-masked, vehicle-controlled and parallel group clinical trials conducted among 35 private eye care clinics in the United States. The studies enrolled 613 participants who were randomized to apply either CSF-1 (n=309) or the vehicle (n=304) twice per day for 2 weeks. The primary endpoint of both trials was the percentage of patients with ≥ a 3-line gain in mesopic distance-corrected near visual acuity (DCNVA), and no loss of ≥ 1-line in CDVA (Monocular Study Eye), which was measured at 1 hour after the first dose on the day 8. The secondary endpoints were measured at 1 hour and 2 hours after the first dose and 1 hour and 2 hours after the second dose on day 8 (a total of four time points).

Participants using Qlosi™ demonstrated significant improvements in their near vision without the loss of ≥ 1 line of DCNVA in the study eye. Within the CSF-1 group, 40.1% of patients demonstrated a response, compared to 19.1% of the vehicle group ($P<0.0001$). For secondary endpoints, most subjects achieved a ≥ 2-line improvement on day 8, and no loss of 1 line or more at distance visual acuity. Qlosi™ recipients also maintained functional near vision from 20 minutes up to 8 hours, as defined by a proportion of participants who achieved 20/40 or better DCNVA.

Finally, binocular summation contributed to a higher achievement of DCNVA versus study eyes alone (Figure 2). Overall, Qlosi™ achieved all primary and key secondary endpoints. Mean scores for drop comfort immediately after instillation on day 1 of the study were 1.5 for the CSF-1 group and 1.0 for the vehicle. All mean values at all time points were below 2. The comfort of the drop scale ranged from 0 (very comfortable) to 10 (very uncomfortable).

Qlosi™ was well tolerated; most adverse events were categorized as mild, transient, and self-resolving. The most common ocular adverse events in the CSF-1 group were

instillation site pain (5.8%), blurred vision (3.6%), conjunctival hyperemia (1.6%), instillation site pruritus (1%), and visual impairment (1%). The most common non-ocular adverse events were headache at 6.8%, instillation site facial pain at 1.9%, and nausea at 1.3%.[2]

**Dr. Gaddie:** Dr. Farid, I've always been fascinated by the variation in effect of miotics on pupil size. Would you talk about the importance of pupil size for maximizing patients' near vision without compromising their distance vision?

**Dr. Farid:** A pupil size of around 2 mm is ideal to improve near vision without compromising distance vision. A very small pupil size of below 2 mm can result in dimming and more visual disturbances.[2,3] Both the NEAR-1 and NEAR-2 trials showed that the 0.4% concentration of pilocarpine provided this improvement in near vision without the mean impact on the distance acuity. In those trials, the optimal pupil size was achieved within 20 minutes of instillation of the drop and persisted across all study days (days 1, 8, and 15).

## LEARNINGS FROM PREVIOUS PRESBYOPIA EYE DROP LAUNCH

**Dr. Gaddie:** Before Qlosi™, there was a first-to-market pharmacological drop for presbyopia correction that wasn't as successful as we clinicians anticipated it to be. Let's discuss what we learned from that launch that will guide our clinical adoption of Qlosi™. Dr. Farid, would you talk about your experience with that previous launch?

**Dr. Farid:** From that launch, we learned the error of making a presbyopic eye drop widely available for any physician, not just ECPs, to prescribe. The key learning was that this type of prescription requires a comprehensive eye examination by ECPs who understand ocular pathology and the requirements for putting patients on these drops.

We also learned a lot about what patients expect from a miotic drop and what they will tolerate in terms of how it feels on the eye and its duration of effect. Patients won't use a drop that feels uncomfortable on their eyes. Similarly, if the drop's effects don't last through the entire workday, patients may discontinue using it, because they don't realize they have the ability to dose again to extend the effect.

Additionally, it's important in this patient population to introduce a miotic drop properly, with instructions for how to instill it and an explanation of how it will alter the vision, its duration of effect, possible side effects, etc. Likewise, patient selection is equally important.

**Dr. Gaddie:** Well said, and I agree with you on the importance of setting patient expectations and proper patient selection. Dr. Quint, what was the impact of allowing practitioners who were not ECPs to prescribe the original formulation?

**Dr. Quint:** As Dr. Farid alluded to, some of the top prescribers of that first drop were not ECPs, but dermatologists and other types of physicians. I think this reflects the broad interest in presbyopia treatments, but practitioners who are not ECPs are not as versed with presbyopia. They don't have the tools to examine the periphery of the retina, evaluate the health of the cornea, or identify ideal candidates. Only ECPs are going to be able to write a prescription for Qlosi™ at launch, which will ensure safe and appropriate prescribing for this drop.

## QLOSI™ PATIENT SELECTION

**Dr. Gaddie:** I agree that if Qlosi™ is going to be as successful as we would all like it to be, we need to identify its best candidates. Dr. Farid, could you talk about suitable criteria for selecting patients who might benefit the most from Qlosi™?

**Dr. Farid:** Qlosi™ is ideal for adult patients with mild-to-moderate presbyopia and especially those who don't want surgical refractive treatments. Qlosi™ is less suitable for patients with advanced presbyopia and those with underlying ocular conditions, such as large pupils with poor elasticity, or retinal pathologies. For these reasons, it is critical for patients to have a comprehensive eye examination to confirm their candidacy for Qlosi™. The patients I will target first to try Qlosi™ are early presbyopes with mild-to-moderate symptoms who aren't necessarily ready for glasses to correct their near vision.

**Dr. Gaddie:** Dr. Quint, I'd like your input on the importance of a thorough patient evaluation and educational discussion.

**Dr. Quint:** Before we prescribe this miotic, it's very important to conduct a thorough eye examination. We need to assess the overall health of the eye, in particular the peripheral retina, the iris, and the cornea. We must identify any underlying pathologies that could

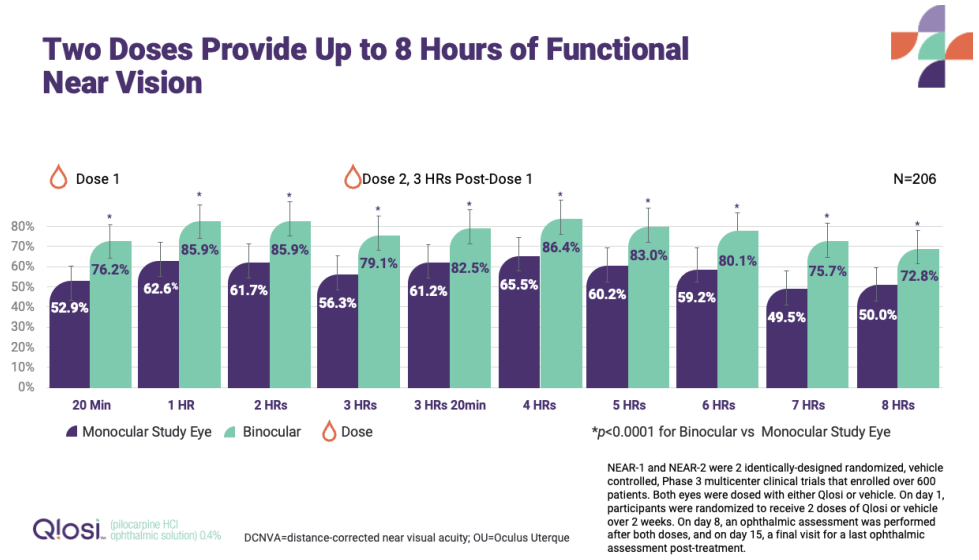


Figure 2. After 2 doses of Qlosi™, functional near vision was extended for up to 8 hours. On day 15, after removing all subjects with a baseline of 20/40 or better OU, there was a statistically significant difference between the DCNVA of study eyes (monocular) versus binocular vision at all time points. Binocular summation contributes to a higher achievement of DCNVA, reflecting real-world vision.[1,2]

1. Cunningham D, Koetting C, Lang J. AOA 2023 ePoster presentation. 2. https://www.optometrytimes.com/view/making-sense-out-of-presbyopia-clinical-study-data. Accessed February 6, 2025.

impact how this medication is going to work or potentially cause an adverse event. That said, I'd like our colleagues to understand that the comprehensive eye examination is sufficient to prescribing Qlosi™ safely.

Then, it's important to explain to potential Qlosi™ patients that there's a difference between improving magnification and improving near vision. We need to clearly explain that Qlosi™ will strengthen near vision without adding magnification.

When I think about the ideal patients for Qlosi™, I'll start with mild-to-moderate presbyopes who are looking for a nonsurgical option. I'm not going to chase a perfect 20/20 outcome, although, if Qlosi™ achieves it, that's great. I want my Qlosi™ patients to have functional vision for their visual needs. The beauty of Qlosi™ is that it has that flexible dosing—it can be dosed once per day or twice per day to give our patients different visual results based on their lifestyle. I believe that clearly understanding their visual goals and appropriately setting their expectations will help ensure our patients' overall success with Qlosi™.

## PATIENT EXPECTATIONS WITH QLOSI™

**Dr. Gaddie:** After using Qlosi™, what should patients' visual experience be? Dr. Farid, what are your expected outcomes and possible side effects with Qlosi™?

**Dr. Farid:** With Qlosi™, patients must understand that they will have a new near point, and it will require some adaptation time. In the Qlosi™ clinical trials, once neuroadaptation occurred, patients' near visual acuity improved. As early as day 1, patients' pupil size constricted and the visual acuity at near improved between day 1 and day 8.

We need to set the expectation for patients that it's going to take a week or 2 for their eyes to adjust and for them to learn the distance at which their near vision will be reset. We must also counsel them that a small number of patients in the Qlosi™ clinical trials experienced mild side effects like headaches and slight burning and stinging during drop instillation. Certainly, these were very tolerable during the clinical trials, but we don't want potential side effects to be a surprise to our patients.

**Dr. Gaddie:** Dr. Quint, could you share with us some of your tips on managing the expectations of our patients? How will you encourage them to continue to use Qlosi™ after their initial experience?

**Dr. Quint:** I love Dr. Farid's idea of the "new near," because the Qlosi™ presbyopia drop is a new innovation, and it's a new experience for our patients. The big advantage of Qlosi™ is that it is a temporary treatment, but when patients first begin using it, they should expect that their distance vision might also look different. Just because it looks different, however, doesn't mean it's a negative impact. Also, this drop makes the pupil smaller, so part of our conversation should include the potential dimming effect versus overall magnification.

## HOW TO GET QLOSI™

**Dr. Gaddie:** Now we'll turn our attention on one of the greatest challenges in all of our practices: how to obtain new treatments once they enter the market. It's always a challenge to figure out the pathway. Dr. Farid, would you please talk about the distribution channels for Qlosi™?

**Dr. Farid:** Qlosi™ can only be prescribed by ECPs at launch and will be available only through specialty pharmacies Medvantx and BlinkRx. We can use our EMRs to send the prescription, and the specialty pharmacy will ship Qlosi™ directly to the patient, ensuring convenience and accessibility. Patients will also receive a welcome kit with their first fill, which will include information regarding their first week of use.

## CONCLUSION

**Dr. Gaddie:** As we've discussed, we have an intriguing new entrant into the pharmacological sector for the treatment of presbyopia with 0.4% pilocarpine in Qlosi™. It has a unique formulation, with a near-neutral pH, and it contains two lubricants. Based on its clinical studies, we expect Qlosi™ to provide excellent near vision without some of the compromises we might expect from traditional pilocarpine.

Qlosi™ achieves an ideal pupil size of 2 to 3 mm and will give our patients a "new near," yet we must be able to articulate to them that Qlosi™ is not a replacement for reading glasses. Rather, it will extend their range of correction for presbyopia.

I'm very excited about the launch of Qlosi™, and I know there will be high interest among our colleagues in having a new eye drop option for treating presbyopia. Thank you, Dr. Farid and Dr. Quint, for joining me today to talk about Qlosi™.

**Dr. Quint:** I think this is a really exciting time for our presbyopia patients. Qlosi™ can offer our patients a solution for their near vision that provides flexible once-a-day or twice-a-day dosing in a preservative-free formulation. And, its availability through specialty pharmacies allows our patients to access this medication in a very personalized way. If our colleagues want to find more additional resources about it, they can go to www.QLOSI.com.

**Dr. Farid:** I'm also excited to have Qlosi™ available now as a nonsurgical solution for our presbyopic patients. I think that having a preservative-free eye drop that has a very low percentage of pilocarpine, and that acts safely and effectively for patients to achieve improved near vision is a win-win.

For us ECPs, we'll have a flexible treatment option to offer our presbyopic patients. By launching Qlosi™ through ECP channels and training providers to perform a comprehensive eye examination on each Qlosi™ candidate, we can ensure safe and appropriate prescribing. I look forward to using it in my clinic. ■

1. For 128 million U.S. presbyopes, doctors of optometry can provide treatment options. American Optometric Association. August 24, 2023. https://www.aoa.org/news/clinical-eye-care/diseases-and-conditions/for-128-million-us-presbyopes-doctors-of-optometry-can-provide-treatment-options?sso=y. Accessed February 24, 2025.
2. Holland E, Karpecki P, Fingeret M, et al. Efficacy and safety of CSF-1 (0.4% pilocarpine hydrochloride) in presbyopia: pooled results of the NEAR Phase 3 randomized, clinical trials. *Clin Ther.* 2024;46(2):104-113.
3. Montés-Micó R, Charman WN. Pharmacological strategies for presbyopia correction. *J Refract Surg.* 2019;35(12):803-814.