Intrepid Eye Society Conversations and Consensus

Shaping the Future of Presbyopic Drops: Clinical Insights and Practical Strategies

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Introduction: Clinical Advances in Presbyopic Drops for Vision Care

Researched and compiled by Janelle L. Davison, OD

Presbyopia remains one of the most ubiquitous visual challenges that eye care providers (ECPs) encounter in clinical practice. As patients reach their fifth & sixth decades of life, the inevitable loss of accommodative amplitude drives them into your chair seeking solutions. Historically, management strategies relied heavily upon optical compensation, primarily through reading glasses, bifocals, or multifocal contact lenses. Surgical interventions, while effective for some, present risk profiles that may make numerous patients hesitant. [NEI 2024]

In recent years, a fundamental shift has slowly and quietly taken place in how we currently approach this condition. Pharmacological management of presbyopia is transforming the landscape of comprehensive eye care. By offering FDA-approved presbyopic eye drops, ECPs can provide a non-invasive, medically driven alternative that meets the demands of a highly active and socially conscious aging population.

The Expanding Presbyopic Demographic

According to the American Optometric Association (AOA), the United States currently has a population that includes approximately 128 million presbyopic patients; demographic projections suggest this number will continue to climb steeply through the year 2030.[AOA HPI 2023] Life expectancy is also steadily increasing, and older adults are remaining active both socially and in the workforce much longer than in previous generations.

This extended period of active living significantly impacts patient expectations. Many individuals find traditional reading glasses frustrating. They easily lose them, resent the constant need to put them on and take them off, and often feel that readers prematurely age their appearance. Multifocal contact lenses offer an alternative, but visual compromises, contrast sensitivity reduction, and dry eye complications frequently limit contact lens tolerance in the presbyopic age group. Additionally, the chair time and costs associated with such expert contact lens fittings often exceed the tolerance of both patients and ECPs.

In our present society, patients actively seek solutions that align with their modern lifestyles. They want to check their smartphones, read digital dashboards, and review menus without reaching for a physical visual aid. Pharmacological presbyopia management directly addresses this massive and motivated demographic.

Mechanism of Action Overview: Modulating Pupil Dynamics

The primary clinical mechanism behind presbyopic eye drops relies on pupil modulation to increase depth of focus. These topical ophthalmic solutions utilize parasympathomimetic agents and/or adrenergic agonists to induce temporary, controlled miosis.[Fricke 2018] By constricting the pupil to an optimal diameter, these drops create a pinhole effect, and this effect fundamentally alters the optical system of the eye.[De Gracia 2025] It reduces peripheral light rays that contribute to spherical aberration, allowing only the central, more focused light rays to reach the fovea. According to De Gracia and Pucker (2025), an optimal pupil size of 2.0–3.0 mm is critical for balancing enhanced near vision with sufficient retinal illuminance. However, potentially reducing the pupil size below 2.0 mm may lead to diminished retinal illuminance, which may impair vision in low-light conditions and compromise overall visual performance. [Xu 2016]

The clinical result of pharmacologic miosis is a significant extension in the depth of focus. Patients' experience improved near and intermediate visual acuity without the need for active ciliary body accommodation. Crucially, this miotic effect achieves enhanced near vision while preserving distance visual acuity. Unlike monovision contact lenses or certain surgical intraocular lens designs, presbyopic drops maintain binocularity. Patients do not have to sacrifice depth perception or distance clarity to read near text. The preservation of binocular distance vision makes this highly appealing option for patients who drive frequently or participate in sports, for example. [De Gracia 2025]

Clinical Evidence and Mechanistic Considerations in Pharmacologic Presbyopia Management

Researched and compiled by Damon Dierker, OD, FAAO & Mary Beth Yackey, OD

Introduction: A Multi-Mechanism Therapeutic Category

Presbyopia is a universal, progressive condition characterized by age-related decline in accommodative amplitude secondary to lenticular stiffening and biomechanical changes within the accommodative apparatus. [Holden 2008] Historically, management has relied on optical correction, including spectacles, contact lenses, or surgical approaches such as corneal inlays and refractive lens exchange.[Wolffsohn 2019]

Currently approved pharmacologic therapies do not represent a single mechanistic class. Instead, available agents employ distinct pharmacologic strategies to achieve functional miosis and improved depth of focus. [Grzybowski 2024] Differences in receptor selectivity, drug concentration, formulation design, and adjunctive receptor modulation may influence onset of action, duration of effect, and physiologic response. Understanding these distinctions is important when interpreting pivotal trial results and considering clinical integration.

Overview of Approved Pharmacologic Agents

Pilocarpine 1.25% (VUITY®)

Pilocarpine 1.25% ophthalmic solution was the first-ever FDA-approved pharmacologic therapy for presbyopia.[VUITY PI] The GEMINI 1 and GEMINI 2 phase 3 randomized clinical trials evaluated once-daily dosing in presbyopic adults aged 40-55 years.[Waring 2022][Lievens 2024] In GEMINI 1, approximately 28-31% of treated participants achieved a ≥3-line improvement in mesopic distance-corrected near visual acuity (DCNVA) at hour 3 in the study eye without losing more than one line of distance acuity, compared with approximately 8-10% in the vehicle group. [Waring 2022] Similar responder rates were observed in GEMINI 2. [Lievens 2024] Near-vision improvement was detectable as early as 15 minutes following instillation and was sustained for several hours in many participants. These trials demonstrated that pharmacologic pupil modulation could provide reproducible, clinically meaningful improvement in near visual acuity for presbyopic patients.

Pilocarpine 0.4% Ophthalmic Solution (QLOSI®)

Pilocarpine 0.4% ophthalmic solution represents a lower-concentration cholinergic miotic formulation developed specifically for the pharmacologic treatment of presbyopia. In contrast to higher-concentration pilocarpine formulations historically used for glaucoma (e.g., 2%), the reduced concentration is intended to achieve effective pupillary constriction while minimizing accommodative spasm and associated adverse effects. [Xu 2016][Holland 2024]

The formulation utilizes a preservative-free vehicle with near-neutral pH designed to enhance ocular surface tolerability and bioavailability. Lubricating excipients including sodium hyaluronate and hydroxypropyl methylcellulose (HPMC) are incorporated to support tear film stability and improve comfort during instillation. [Xu 2016][Holland 2024][QLOSI PI]

The efficacy and safety of pilocarpine 0.4% were evaluated in the pivotal NEAR-1 and NEAR-2 phase 3 clinical trials. These randomized, double-masked, vehicle-controlled studies enrolled adults with presbyopia across a well-defined range of both age and refractive error. A total of 613 participants were randomized, with 309 receiving pilocarpine 0.4% and 304 receiving vehicle control. Participants were dosed bilaterally twice daily for two weeks, with the second dose

administered approximately 2-3 hours after the first. Ophthalmic assessments were performed on study days 1, 8, and 15. [Holland 2024]

The primary efficacy endpoint for NEAR-1 and -2 was the proportion of participants achieving a ≥3-line improvement in mesopic, distance-corrected near visual acuity without a clinically meaningful loss of corrected distance visual acuity in the study eye. Across pooled analyses, pilocarpine 0.4% demonstrated statistically significant improvement compared with vehicle at multiple post-instillation time points. At one hour after the first dose, 40.1% of treated participants achieved the ≥3-line responder endpoint in the study eye, as compared with 19.1% in the vehicle group. After the second dose, responder rates increased to 49.5% compared with 16.1% in the vehicle group ($p < 0.0001$). [Holland 2024]

Treatment effects were typically observed within the first hour following installation and were reproducible across dosing days. Improvements in binocular near vision were also observed, supporting functional benefit for common near-vision tasks. [Cunningham 2023]

***Aceclidine 1.44% Ophthalmic Solution* (VIZZ™)**

Aceclidine is a selective muscarinic agonist with high affinity for M3 receptors and a pharmacologic profile distinct from other miotic agents.[Özyol 2025] Though never approved or marketed in the US prior to 2025, aceclidine was available in Europe for glaucoma as far back as 1970, and sold by Chibret under the brand name Glaucostat.[Mullard 2025] Its distinguishing feature relative to pilocarpine and carbachol was always its more favorable accommodative profile, as early clinical work suggested that aceclidine produced the least effect on accommodation among the miotics studied.[Fechner 1975]

The efficacy and safety of aceclidine were evaluated in the pivotal CLARITY-1 and CLARITY-2 phase 3 clinical trials. These randomized, double-masked, controlled studies enrolled presbyopic adults within a well-defined range of both age and refractive error, including individuals who were post-refractive surgery or pseudophakic. The primary efficacy endpoint was the proportion of participants achieving a ≥3-line improvement in high-contrast, monocular, distance-corrected near visual acuity (DCNVA) at 3 hours post-instillation on day 1, without loss of ≥1 line of distance visual acuity. [VIZZ PI]

Across the CLARITY phase 3 trials, approximately 71% of treated participants achieved the primary endpoint at 3 hours compared with about 8% of participants receiving vehicle, demonstrating a substantial treatment effect at the prespecified primary assessment time point. [VIZZ PI] Improvements in near visual acuity were observed as early as 30 minutes following instillation and remained high during the early post-dose interval.

The treatment effect gradually declined over time but remained measurable throughout the evaluation period. Across phase 3 trials, 27-40% of treated participants maintained a ≥3-line improvement in photopic, monocular DCNVA at 10 hours post-instillation. [VIZZ PI]

Carbachol 2.75% / Brimonidine 0.1% Ophthalmic Solution (YUVEZZI™)

Carbachol/brimonidine ophthalmic represents the first fixed combination solution in the presbyopia-management category, joining muscarinic stimulation with alpha-2 adrenergic agonism.[YUVEZZI PI] Carbachol induces iris sphincter contraction producing pupillary constriction, while brimonidine inhibits sympathetic-mediated dilation of the iris dilator muscle.[Abdelkader 2015][Tatsui 2016] This dual-mechanism strategy is intended to enhance the magnitude and stability of pharmacologic miosis.[Abdelkader 2016][Hom 2021]

The efficacy and safety of this combination therapy was evaluated in the BRIO clinical development program, which included two multicenter randomized phase 3 trials (BRIO I and BRIO II) enrolling the broadest age range of presbyopic adults (45-80 years), and including both phakic and aphakic functional emmetropes.[YUVEZZI PI][Visus 2023][Tenpoint 2025] The primary endpoint of these studies was the proportion of participants achieving ≥15-letter (≥3-line) improvement in binocular uncorrected near visual acuity without loss of ≥5 ETDRS letters of distance visual acuity.

In BRIO I, the combination therapy demonstrated statistically significant superiority compared with both carbachol and brimonidine monotherapies at key post-instillation time points, with durable miosis observed for up to 10 hours. [Visus 2023] In BRIO II, the primary endpoint was achieved at multiple time points including 0.5 through 8 hours following dosing.[Tenpoint 2025]

Interpreting Efficacy and Safety Across Clinical Trials

Although all approved pharmacologic agents demonstrated statistically significant improvement in near visual acuity compared with vehicle, cross-trial comparisons should be interpreted cautiously.

Clinical trials differed with respect to:

- age and demographic distribution
- baseline refractive error limits
- testing conditions (photopic vs mesopic illumination)
- study duration
- dosing frequency
- primary endpoint
- timing of outcome measures
- use of monocular versus binocular visual acuity endpoints

These methodological differences may influence responder rates and should be considered when interpreting reported outcomes, lest the results be interpreted as evidence of superiority. A listing of these key measurements is included in **Table #1**. Likewise, safety measures may be interpreted differently by individual subjects, and reporting is dependent upon both patients and

researchers. A listing of comparable adverse events from the various trials is presented in **Table #2**.

Interpreting Efficacy in Terms of Functional Vision

Regardless of the wide disparity in clinical trial design and outcomes for the various products mentioned above, one outcome measure that has been consistently identified and discussed across this category is the potential for attainment of binocular 20/40 visual acuity. For the GEMINI series, achieving 20/40 or better in **photopic**, high-contrast, binocular DCNVA at Day 30, Hour 3 was a prespecified secondary endpoint. Approximately 9 out of 10 participants using pilocarpine HCl 1.25% achieved this threshold (84.5% in GEMINI-1 and 90.2% in GEMINI-2). [Waring 2022][Lievens 2024]

In the case of pilocarpine HCl 0.4%, a post-hoc study using pooled data from NEAR-1 and NEAR-2 revealed that, under binocular conditions, the proportion achieving 20/40 or better ranged from approximately 76% at 20 minutes post-dose 1 to roughly 86% at 1–2 hours, and remained at approximately 73% at 8 hours post-dose 2. However, there are two important caveats to note here: (1) the analysis excluded all subjects whose DCNVA was 20/40 or better at baseline, resulting in a cohort of 206 subjects (vs. 309 total); and (2) these data, as all data from the NEAR series, were obtained under **mesopic**, rather than photopic conditions.[Cunningham 2023]

CLARITY-1 & CLARITY-2 showed similar results for aceclidine 1.44%. In those pooled trials, 93% of participants achieved functional near vision outcomes of 20/40 (J3) or better DCNVA under binocular, **photopic** conditions on Day 1 at 30 minutes, while approximately 7 out of 10 patients (69%) maintained this threshold at 10 hours.[Eiden 2023] Finally, BRIO-1 reported the proportion of subjects achieving 20/40 or better in binocular, uncorrected near visual acuity (BUCNVA) under **mesopic** conditions across 10 hours in the full population of 182 emmetropic subjects for carbachol 2.75%/brimonidine tartrate 0.1%. The results demonstrated 20/40 or better acuity was achieved by 74% of subjects at 30 minutes post-dose, with a peak rate of 85% at hour 1, 56% at hour 8, and 49% at hour 10.[El-Harazi 2025] Consistent with our previous discussion, however, the uncorrected binocular design of BRIO reflects the strict emmetrope-only enrollment criterion, which makes these 20/40 rates not directly comparable to the distance-corrected binocular rates reported by GEMINI and CLARITY, nor to the post-hoc figures from NEAR.

Mechanistic Imaging Insights Regarding Pilocarpine

Given the relatively recent emergence of this therapeutic category, it is no surprise that there is a scarcity of evidence beyond the clinical trial data to inform our decisions at the present time.

Clinicians may rely on a variety of factors when determining which agent to prescribe in a given scenario; these may include patient feedback, personal experience, and individual patient expectations, among other factors. However, we must ultimately look to well-designed, real-world post-market studies to guide our decision-making.

One such study that bears further examination was recently presented at an international ophthalmology conference in early 2026.[Cabot 2026] Researchers at the Bascom Palmer Eye Institute utilized a high resolution, synchronized, dual optical coherence tomography (OCT) system with dynamic imaging capability for both the anterior segment (AS) and ciliary muscle (CM) to investigate anatomical changes associated with accommodation. Their complex system incorporated an internal fixation stimulus that prompts the eye to actively focus, permitting researchers to image the eye's accommodative mechanism in real time by using a dichroic mirror to merge the imaging and stimulus light paths without interference.[Ruggeri 2016]

Candidates for the study were required to meet the following criteria: 45 to 64 years of age; <4D of myopia (spherical equivalent); no history of intraocular surgery, PRK/LASIK, retinal detachment, glaucoma or any other ocular condition that in the opinion of the researchers might impact the study results. In addition, all candidates underwent a preliminary imaging session using the proprietary CM-OCT system to assess the visibility of the ciliary muscle, ensuring sufficient resolution to enable muscle thickness measurements.

Researchers hypothesized that the use of a low-concentration pilocarpine – in this case, QLOSI (0.4% pilocarpine HCl) – would have a diminished effect on the ciliary muscle as compared to a higher concentration of the drug. To demonstrate this, subjects (n=10) underwent three sessions with the dual OCT system, each separated by approximately one week. At each visit, OCTs of the pupil, lens, and ciliary body were captured before and one hour after instillation of a topical agent, in the following order: (1) balanced salt solution (BSS) as a negative control; (2) QLOSI (0.4% pilocarpine HCl); and (3) 2% pilocarpine HCl as a positive control. Imaging consisted of static AS-OCT, static CM-OCT, and dynamic CM-OCT, each conducted with fixation at distance (6 m) and near (40 cm). A total of 28,800 images were recorded, from which over 12,000 were incorporated into the final analysis.

The results of this study were consistent with the original hypothesis: low-concentration pilocarpine, i.e., QLOSI, appears to have a markedly reduced effect on the ciliary muscle as compared with higher-concentration pilocarpine. Indeed, from the standpoint of statistical significance, the impact of low-concentration pilocarpine on ciliary muscle thickness was comparable to BSS. Additional results from the study demonstrated concentration-dependent pupil constriction for pilocarpine; miosis with low-concentration pilocarpine was statistically less than high-concentration pilocarpine, but greater than BSS. Finally, a negligible impact on lens thickness was seen with low-concentration vs. high-concentration pilocarpine, particularly at near.

These findings challenge long-held beliefs about the unavoidable accommodative effects of pilocarpine and moreover help to establish pupil selectivity as a concentration-dependent attribute of this drug. For decades, pilocarpine has been defined by its mutual, simultaneous action on the iris sphincter and ciliary muscle, a concept that has limited its use in presbyopia due to the potential for brow ache, accommodative spasm, induced myopia, and even concerns regarding vitreoretinal traction. Understanding this mechanistic distinction associated with pilocarpine's concentration also helps to better frame the historical concern regarding risk of retinal detachment, which persists to this day. [Elhusseiny 2025] At higher concentrations, we know that pilocarpine induces strong ciliary muscle contraction, in turn causing anterior displacement of the lens-iris diaphragm. This forward movement can increase tractional forces on the vitreous base, which is of significantly greater concern in eyes with pre-existing risk factors for retinal detachment such as lattice degeneration, high myopia, or peripheral retinal thinning. Considering this new research from Bascom Palmer, however, one can make the mechanistic argument for a diminished theoretical risk profile in favor of low-concentration pilocarpine, in terms of both ciliary muscle related symptoms and potential retinal detachment. Indeed, to coin a phrase… all pilocarpine is not created equal as it pertains to presbyopia management.

Key Implications

- The emergence of pharmacologic presbyopia therapies represents a meaningful expansion of the refractive management continuum. Evidence from multiple pivotal trials demonstrates that pharmacologic pupil modulation can provide clinically meaningful improvement in near visual acuity while preserving functional distance vision.
- Differences in pharmacologic mechanism, drug concentration, and receptor selectivity introduce physiologic diversity within the category. Understanding these distinctions supports appropriate patient selection and informed clinical counseling.
- As additional real-world data and comparative studies emerge, further insight into durability, performance across various lighting levels, and patient-reported outcomes will refine the role of pharmacologic presbyopia therapy within contemporary refractive care.
- Pharmacologic presbyopia therapies may serve as an important addition to the refractive care continuum, providing another noninvasive option that complements existing strategies such as spectacles, contact lenses, and refractive surgery.

Practicality in Prescribing for Presbyopia Pharmaceuticals: Consideration of Side Effect Profiles

Researched and compiled by Mark Buboltz, OD, FAAO

Since the FDA approval of VUITY (pilocarpine HCl 1.25%) in late 2021, the presbyopia-drop category has matured quickly. What began as a one-product conversation is now a true therapeutic class, with a total of four FDA-approved options available in the United States, including QLOSI (pilocarpine HCl 0.4%), VIZZ (aceclidine 1.44%), and YUVEZZI (carbachol 2.75%/brimonidine tartrate 0.1%), as well as additional products in development.[VUITY PI][QLOSI PI][VIZZ PI][YUVEZZI PI] More treatment options should theoretically make prescribing easier, however that is not always the case. As the number of choices grows, so can the paradox of choice. Many eye doctors are now left asking a deceptively simple question: *Which drop should I initially select for most of my patients?* Having multiple options is useful only if those options can be organized into a rational prescribing strategy. The good news is that when clinical trial data (via package inserts) are viewed alongside early real-world experience, a clearer hierarchy begins to emerge.

The first principle is straightforward: presbyopia drops should be prescribed like true pharmacologic therapies, not treated as casual lifestyle enhancers. All currently available agents work primarily through pupil modulation, and hence each of them comes with some version of the same counseling for patients: a discussion about potential blurring or dimming of vision, headaches, and instillation site irritation. In elective therapy, patients do not judge success solely by near acuity gains; rather, they evaluate the drop's convenience and tolerability as much as, if not more than, its efficacy.

That point leads to the second principle: in presbyopia care, tolerability is not secondary to efficacy; it is a critical element of efficacy. A medication that improves near vision but induces stinging, redness, dimming, or headache to the extent that it discourages continued use is not a practical success. This is especially true in the "cash-pay" category, where patients have low tolerance for side effects and little incentive to "push through" discomfort or long bouts of conjunctival hyperemia. For many patients, the first experience with a presbyopia drop often determines whether they continue or even consider the category a second time. That is why the most effective prescribing strategy is not to start with the strongest or longest-lasting drug, but rather with the option most likely to deliver benefit with the least amount of friction.

Before sorting through the differences among products, one shared safety issue deserves emphasis: miotic therapy is not entirely benign. All of the currently available products in this category carry similar warnings about retinal complications, including retinal tears or detachments in susceptible patients.[VUITY PI][QLOSI PI][VIZZ PI][YUVEZZI PI] Patients with high myopia, lattice degeneration, prior retinal tear or detachment, symptomatic posterior

vitreous detachment, or unexplained flashes and floaters merit a more deliberate conversation and caution before treatment is initiated. Presbyopia drops should not be prescribed reflexively without first performing a thorough ocular health exam. With safe patient selection such as those patients included within the demographics of the clinical trials, the risk of retinal detachment is extremely low, with none of the newer medications reporting retinal detachments within their clinical trial patient cohorts.

With that framework in place, the key question becomes more practical: considering safety and tolerance of these medications, which of the available options is most appropriate as first-line therapy? On current evidence, QLOSI makes the strongest case, and we will outline why this is so important.

The reason for this statement is not that QLOSI has proven to be superior in any head-to-head randomized trials, since no such studies have been published to date. Instead, the reason is that QLOSI appears to offer the most balanced combination of efficacy, tolerability, and flexibility within the current field. Its package insert reports an arguably modest adverse-event profile, with the most common reactions in the 5%–8% range, particularly headache and instillation-site discomfort, with blurred vision reported less commonly. [QLOSI PI]

While a long-standing concern for pilocarpine use has been its effect on the ciliary body, leading to headache, myopic shifts, and the potential for retinal implications, the recent work by Cabot and associates out of Bascom Palmer Eye Institute suggest that pilocarpine 0.4% induces a ciliary muscle accommodative response comparable to balanced salt solution (BSS) control, and significantly less than the 2% pilocarpine studied.[Cabot 2026] In a category where comfort determines adoption, formulation matters.

That favorable impression is supported by the pooled phase 3 NEAR data. In those trials, pilocarpine 0.4% improved near vision without compromising distance vision and did so with a favorable safety profile, with no serious or severe treatment-related adverse events (AEs), including no retinal detachments reported in the published analysis.[Holland 2024] By contrast, the months following VUITY's launch were plagued by instances of retinal detachment purportedly associated with that particular medication.[Elhusseiny 2025][Al-Khersan 2022][Eton 2024][Eaddy 2024][Singh 2025]To its credit, QLOSI has seen no noted retinal detachments in the roughly one year since its launch (April 2025), according to the FDA Adverse Event Monitoring System (AEMS).[FDA 2026] This AE data supports the practical impression that concerns most clinicians: QLOSI appears to deliver significant visual benefit without asking patients to accept a disproportionately burdensome drop experience.

Now that the point has been made delineating why QLOSI should be considered first line among pharmaceutical agents for presbyopia, the rest of the category begins to sort itself more naturally.

VIZZ is a presbyopia medication that stands out for its potency and duration. For patients who want sustained near benefit and are willing to accept a more noticeable drop experience, VIZZ

may be highly attractive. However, that benefit comes with a greater tolerability tradeoff. Its prescribing information reports substantially higher rates for instillation-site irritation, dim vision, headache, and hyperemia. [VIZZ PI] Comparatively higher AEs must always be a consideration in medicine, and this is especially true of an elective medication for presbyopia.

Just as importantly, VIZZ's launch illustrated why AEs listed on package inserts do not always tell the whole story. After launch, redness appears to have become one of the more clinically salient counseling points surrounding the drug. In the original trial data, hyperemia was noted to be present in 7-8% of patients after 30 minutes of instillation; [VIZZ PI] however, real world experience has proven this to be much higher, especially within the first 30 minutes of administration. This reflects the reality that some adverse events matter more once a drug is used in everyday settings by image-conscious, socially active, and symptom-sensitive patients.

YUVEZZI – the newest entry into this therapeutic space – occupies yet another position in the hierarchy. Its carbachol/brimonidine combination gives it a distinct pharmacologic profile, and its once-daily dosing will appeal to patients who prioritize simplicity in their regimen. Its development program also included a significant percentage of pseudophakic and post-refractive surgery patients, making it relevant to a broader swath of contemporary practice. [YUVEZZI PI] Yet the same pattern appears again: the package-insert tolerability burden is not trivial. Eye pain upon instillation and visual impairment occurred in more than 5% to 7% of participants, while eye irritation upon instillation and headache occurred in more than 10% to 16%. [YUVEZZI PI]

In our collective view, VUITY has now been rendered obsolete by this new wave of presbyopia drops, although it deserves credit for proving that a market for pharmacologic presbyopia treatment exists. For this reason, we will not dwell on the AE profile related to VUITY. A summary of AEs for all approved agents in this category is presented in **Table #2**.

Taken together, these observations suggest that presbyopia-drop prescribing should become stepwise rather than brand-driven. We recommend starting with the option that is safest, most comfortable, and easiest to adopt, and escalating therapy only when the patient's individual goals demand more than what the initial selection can provide. For the average early or moderate presbyope, those interested in more flexible dosing or concerned about side effects should start with QLOSI. For the patient who wants greater duration and is willing to accept the increased likelihood of irritation, dimming, or redness, consider VIZZ. For the patient who requires the longest possible duration of action and appreciates the dual-mechanism approach, consider YUVEZZI. Finally, while VUITY may still have a potential role in selected situations, especially where historical experience drives the choice. Nonetheless, given the improved safety and efficacy of this second generation of presbyopia drops, VUITY has been fundamentally eclipsed by the newer formulations.

The expansion of presbyopia drops should not lead to therapeutic paralysis. If anything, it should allow clinicians to prescribe more thoughtfully. Clinical trials remain the foundation, but real-world experience reveals what truly motivates patients: comfort, redness, headache, dim vision,

retinal safety, and whether the drop still feels worth using after the novelty fades. When those practical realities are given appropriate weight, the current field becomes much easier to categorize. In summary, it's not that the category needs fewer choices. Rather, it needs a clearer starting point, and based upon our research and consensus, QLOSI appears to represent the most favorable first step.

Patient Selection Considerations for Presbyopia Drops

Researched and compiled by Mark Schaeffer, OD, FAAO

While presbyopia itself affects every individual once they reach a certain age, not every management strategy delivers effectively for every patient. When pharmacological options entered the therapeutic space to enhance near vision, identifying the "right" patient became paramount to their success. Of course, it's important to cast a wide net since presbyopia affects every individual somewhat differently. The world in which the patient lives can have a wide variety of near targets, complaints, and lifestyle needs. This means that eye care professionals must take a few extra steps to demonstrate the experiential value of using eye drops to enhance near vision. What each patient deems a success depends upon the expectations set by the prescribing doctor and the usage that the patient envisions.

When expectations are set, it is paramount to highlight what the drops can do without overpromising, while simultaneously refraining from discouraging patients by implicating too many compromises. Explain that the drops are designed to *reduce the patient's reliance on reading glasses* to improve functionality. There are patients who need sharp, clear vision for which these options work well, and there are others just looking for a boost in their natural vision to help alleviate strain and symptoms. The difficult part can be screening these patients if there is no protocol or education in place to identify good candidates.

As an initial step, each patient candidate must undergo a comprehensive eye examination and fundus evaluation to assess pupillary anatomy and screen for any relevant pathology. Those at risk of complications, or in whom the drops may underperform due to baseline characteristics, must be informed and gently dissuaded. For all others, the relevant risks, benefits, and potential side effects of the medications should be disclosed and delineated. Regardless of the adverse event rates in clinical trials, patients should know what to expect if something happens to them. When prescribers fail to set appropriate expectations, the patients set their own, and this can lead to failure and non-compliance, especially for those who are new or returning to vision correction.

The correct verbiage can also make or break the patient experience, both in and out of the exam room. Whether a practice doses in-chair, dispenses a sample, or goes straight to prescribing, helping the patient understand the process, timeline, and potential side effects ensures

comprehension and future motivation. Current best practices include setting realistic expectations for what the patient's vision could resemble post-instillation. Avoiding terms like "*cure*" or "*replace*" and instead using phrases like "*reduce reliance*" or "*gain functionality*" goes a long way toward ensuring patient success.

Approaching Various Patient Types

Treatment-naive presbyopic patients. These individuals have never experienced consistently blurry vision prior to the onset of presbyopia. They may not have even undergone an eye exam as an adult, or in decades. Such patients present a great opportunity to showcase the whole menu of options, including glasses, contact lenses and presbyopia drops. Since these patients have never required correction, their knowledge of current therapeutic options is often drastically limited. While it's likely they've seen (or even used) over the counter readers, and may even be familiar with progressives through a friend or relative, they will often express some degree of apprehension and may have many questions. Likewise, they will probably be even less familiar with contact lenses, including the concept of monovision or simultaneous vision using multifocal designs.

For patients of this variety, it is best to explain the mechanics of creating depth of focus with presbyopia drops, and how this helps to improve near vision without the need for readers or other mechanical devices. Emphasize that these drops leverage the eye's natural optics to improve their functional near vision.

Patients with a low Rx, currently wearing some type of correction but looking for additional flexibility. The patient who is fortunate enough to have a mild Rx (i.e., between -0.50D and +1.50D at distance) has a great variety of options. With today's technology, one can easily shift between glasses and contact lenses and now employ pharmaceutical options as well. Offering the choice of different corrective measures on any given day can promote greater overall satisfaction with their vision, simply because they are no longer beholden to any single option. People are generally resistant to change thrust upon them, but if there is autonomy in the decision, they are more likely to embrace it.

For these patients, introduce an alternative option designed to provide both functionality and flexibility. The option of presbyopia drops may be beneficial to them for such things as hobbies and social functions, exercise and physical activities, or just weekend use. Permit and encourage these patients to try the drops for a week or two, to learn precisely how and where they are best utilized.

Post-LASIK patients. Patients who have undergone refractive surgery have already demonstrated a desire to reduce their reliance on glasses and contact lenses, expressing a willingness for out-

of-pocket options to gain freedom from corrective devices. These individuals truly want an untethered approach to vision and can be great candidates for pharmacological presbyopia therapy. In these scenarios, provide education on the value of reducing the need for corrective lenses, while underscoring the enhanced flexibility associated with drop therapy. Remember, however, to consider the presurgical refraction (and/or biometry measurements) in these patients, to rule out high axial myopes who may be at greater risk for retinal compromise. Similarly, always perform a careful and thorough retinal evaluation in consideration of previous refractive error to identify any additional pathological risk factors.

Pseudophakic patients. Post-cataract surgery patients are typically corrected for distance, providing clear vision without the need for a full-time prescription. Many of them have been wearing prescription glasses or readers for decades and are likely unaware of the current options. These individuals understand near vision challenges better than most, and while they may have no objections to wearing glasses and/or contact lenses in most situations, it is possible that they are also looking for something to provide greater flexibility and freedom.

For these patients, setting appropriate expectations is essential. While clinical studies refer to the number of letters or lines gained, the patient's experience is much more goal-oriented: Can I see it comfortably or not? Emphasizing functionality over precise vision can help better summarize the results for these patients. In many cases, the patient may not require perfect 20/20 acuity at near, but would simply like to improve their vision without corrective devices to enhance their quality of life.

Multifocal or monovision contact lens wearers. Multifocal optics have improved dramatically over the past decade, achieving high success rates with first- and second-lens options. Nonetheless, there are still finite lens parameters, as well as patients that simply do not adapt well to those optical designs. In many cases, these patients are determined not to wear glasses under any circumstances; hence, pharmaceutical intervention can be a great tool to improve near vision in such individuals. When dealing with these patients, discuss the concept of small pupil optics and how it differs from simultaneous vision associated with multifocal contact lenses, or the unique visual experience associated with monovision. Moreover, determine whether the drops will be used in conjunction with or as an alternative to contact lenses. For those employing lenses and drops simultaneously, always review the need to wait at least 10 minutes between drop instillation and insertion of the lenses. Regardless of the product used, this patient counseling information is consistent across all currently approved drops in the category.

Key Implications

Overall, many patients who present routinely to eye care clinics may qualify as good candidates for presbyopia drops. While they may possess different experiences, motivations, desires and expectations for a topical therapy, the prescriber can never be sure of the patient's level of

interest unless the option is presented alongside the proper expectations, risks, and benefits. Some patients who appear to be ideal candidates may reject the idea outright, while other seemingly less likely candidates may be highly intrigued and enthusiastic toward such an option. Realize too that, for most patients that present for an ophthalmic examination, the challenge is simply knowing where to start the conversation with their doctor about pharmaceutical options.

We recommend starting with a simple prompt: "*As well as glasses and contact lenses, there are new options to help improve your near vision by using prescription eye drops. What are your thoughts? Would you like to know more?*" While it may sometimes feel like a waste of time having this discussion with every potential candidate, at least those patients will leave with the knowledge that their doctor is presenting all options, and initiating a conversation rather than making a foregone conclusion. It may be surprising to learn just how many patients are excited about using novel therapy to help them live a life free from continued reliance on glasses or contact lenses.

Integrating into Practices: Considerations for Primary Care

Researched and compiled by Janelle L. Davison, OD

Integrating presbyopia drops into a primary eye care practice offers an exciting opportunity to provide patients with innovative, non-invasive solutions for managing their near vision challenges. However, successful implementation requires careful planning and a strategic approach to address clinical, operational, and patient education aspects. As stated previously, one of the primary challenges in implementing presbyopia drops is appropriately managing patient expectations. While these drops can significantly improve near vision, they are not a cure for presbyopia and may not eliminate the need for reading glasses in all situations. Patients should be informed about the temporary nature of their effect and the potential for associated side effects. Clear communication about these limitations can prevent dissatisfaction and build trust. Proper patient selection is also crucial, as not all individuals will benefit equally from presbyopia drops. For instance, patients with central corneal opacities or irregularities may experience suboptimal results. Establishing clear inclusion and exclusion criteria within the practice can streamline the prescribing process and improve outcomes.

Gaining staff buy-in is another critical component of successful implementation. Educating the team on the science behind these therapies, including how they work and their benefits, is essential. Hosting a "lunch-and-learn" session with vendor representatives can provide in-depth training and help answer questions, ensuring that the staff feels confident discussing these options with patients. Empowering staff to identify potential candidates during pre-testing and to educate patients about the therapy during their visit can enhance patient trust and further

accelerate the process. Providing scripts or frequently-asked-questions (FAQs) for staff to use when patients inquire about the drops can also ensure consistent messaging. For example, a technician might explain, "*These drops can help you see up close without glasses for several hours, and they're a great option if you're looking for a non-invasive solution!*"

Educating patients about presbyopia drops should be a defined yet comprehensive process. Visual aids, such as brochures or videos, can effectively explain how the drops work and what patients can expect. Highlighting key benefits such as improved near vision without compromising distance vision or depth perception can help patients understand the value of this therapy. During consultations, it's equally important to address common concerns such as safety and side effects. Creating a dedicated "presbyopia educational center" in the office, where patients can watch a short video or review educational materials while waiting, can save chair time and further ensure consistent messaging.

Partnering with vendor representatives can provide additional, valuable resources to bolster the integration of presbyopia drops into your practice. Many vendors offer patient starter kits that include sample drops, educational materials, and instructions for use. These kits allow patients to experience the benefits of therapy firsthand, increasing their likelihood of adherence. Vendor representatives can also assist with staff training, patient education materials, and marketing support, such as posters or digital content for your website, as well as social media channels to promote the availability of presbyopia drops in your practice.

Facilitating neuroadaptation is another critical consideration. Patients need time to adjust to the new visual experience provided by presbyopia drops, just as they would with new progressives or multifocal contact lenses. Providing clear guidance on what to expect during this period is crucial. For example, you might explain, "*It may take several days to a week for your brain to fully adjust to these changes in your vision. During this time, you might notice slight differences in how you see both up close and at a distance.*" Starter kits provided by vendors typically include detailed instructions and tips for maximizing the benefits of the drops, such as using them consistently at the same time each day. Suggest patients adhere closely to the recommended regimen to obtain maximal results and expedient adaptation.

To ensure more long-term success, we recommend establishing a system for tracking patient outcomes and satisfaction. Follow up with patients after their initial use of the drops to address any concerns and gather feedback. This not only helps refine your prescribing process but also demonstrates your commitment to patient care. Consider implementing a short survey to assess patient satisfaction and identify areas for improvement. Questions might include, "*How satisfied are you with your near vision after using the drops?*" and "*Would you recommend this therapy to others?*".

By addressing clinical considerations, educating staff and patients, and leveraging vendor partnerships, optometrists can successfully integrate presbyopia drops into their practice while minimizing potential pitfalls. With careful planning and a patient-centered approach, presbyopia

drops can become a valuable addition to your practice's offerings, enhancing both patient satisfaction and practice growth.

Integrating into Practices: Considerations for the Dry Eye Clinic

Researched and compiled by Mark Buboltz, OD, FAAO

Specialty dry eye clinics represent a natural and logical setting in which to integrate presbyopia drops. Many patients in a high-volume dry eye practice already fit the demographic most likely to benefit from pharmacologic presbyopia treatment: they are often between 45 and 60 years old, symptomatic with near-task frustration, and highly motivated to improve day-to-day visual function. Rather than viewing presbyopia drops as outside the dry eye channel, they should be thought of as a practical extension of comprehensive ocular surface and functional vision care.

This fit becomes even more compelling when considering the types of patients commonly seen in specialty dry eye clinics. These practices often care for a disproportionate number of individuals with contact lens intolerance, fluctuating vision, and post-refractive surgery complaints. Those same patients are often looking for spectacle independence or reduced reliance on readers, making them especially good candidates for presbyopia drop discussions. Such examples may include post-LASIK patients who are emerging presbyopes, or those who have reduced or discontinued contact lens wear because of associated dryness.

The key to success is proper sequencing and positioning. In a dry eye clinic, presbyopia drops should be promoted not as a replacement for ocular surface treatment, but rather as an adjunctive therapy once the surface has been optimized. Tear film instability alone can degrade near vision and create fluctuating blur, so initiating a presbyopia drop on an inflamed or unstable ocular surface may lead to further symptoms and complication of the clinical picture. Once the surface is improved, however, the patient is in a far better position to appreciate the benefits of presbyopia drops, and to judge their efficacy and tolerability more accurately.

This approach also aligns well with the broader philosophy of specialty dry eye care. These clinics are already committed toward improving quality of life, visual performance, and comfort, rather than simply treating a disease. Presbyopia management fits naturally into that model; it provides the clinician another way to help patients function better at work and in social settings, whether they are reading, using digital devices, or engaging in other active pursuits.

Within such a framework, presbyopia drops become less of a separate category and more of a next-step offering for the right patients. For those in a specialty dry eye clinic, this concept is both clinically sensible and strategically valuable: treat the surface first, stabilize the visual

system, and then consider pharmacologic support for near vision in patients whose symptoms and goals make them good candidates.

Integrating into Practices: Considerations for Eye Care Aesthetics

Researched and compiled by Janelle L. Davison, OD

Integrating aesthetic services into an advanced dry eye practice is a natural progression for eye care professionals, particularly when treating patients in the presbyopic age range. Technologies like intense pulsed light (IPL), radiofrequency (RF), and dynamic muscle stimulation not only address the underlying causes of dry eye but also provide aesthetic benefits, such as reducing redness, improving skin texture, and tightening the skin around the eyes.[Betz 2025][Tichenor 2025] For many of these patients, however, the first noticeable sign of aging isn't simply their appearance, but rather their vision. Presbyopia is most assuredly a significant concern for this demographic. By incorporating presbyopia drops into the treatment menu, eye care professionals can offer a comprehensive approach to managing both the aesthetic and functional aspects of aging.

Accordingly, patients seeking aesthetic treatment are often proactive about their health and appearance, making them generally good candidates for presbyopia drops. These individuals are seemingly invested in improving their appearance and are likely to appreciate the convenience and innovation of a less intrusive solution for their visual needs. To successfully integrate presbyopia drops, a strategic and patient-centered approach is essential.

To streamline the integration of presbyopia drops, consider bundling them with advanced dry eye treatments. For example, patients undergoing IPL or RF therapy could receive a complimentary starter kit of presbyopia drops as part of their care plan. In these cases, we suggest starting with the lowest concentration miotic drop to minimize adverse events while introducing the patient to the concept of therapeutics for presbyopia. This approach introduces patients to the benefits of the drops while reinforcing your practice as a comprehensive provider of age-related care.

By addressing both the functional and aesthetic aspects of aging, eye care professionals can create a comprehensive approach that enhances patient satisfaction and loyalty. Integrating presbyopia drops into an existing aesthetics setting expands treatment offerings while positioning your practice as a leader in innovative, patient-centered care. With careful planning and a strategic approach, presbyopia drops can become a valuable addition to your treatment menu, helping patients see and feel their best at any age.

Integrating into Practices: OD/MD Surgical Clinic

Researched and compiled by Nick Bruns, OD, FAAO

In surgical settings, pharmaceutical pupil modulation offers a unique opportunity to extend functional vision both pre- and postoperatively. Consider these common scenarios:

An early presbyopic patient with no distance correction presents for a refractive surgery consultation. Prior to presbyopia drops, these were uncomfortable encounters forcing serious compromise - monovision, partial correction, or simply deferral of surgery altogether. With pharmaceuticals as a refractive management category, physicians are armed with a non-invasive and reversible option to treat an untapped patient demographic.

A cataract patient considering presbyopia-correcting IOLs, but hesitant to undergo surgery. Pharmaceuticals can act as a bridge strategy; by enhancing the clear range of vision pharmacologically, patients may maintain high-quality function while preserving the option to pursue surgical intervention when they are ready.

A patient who elected a presbyopia correcting IOL but is still unable to read small print, especially in low light. Despite advancements in IOL design, we still do not have a true accommodating IOL. Current designs either split or stretch light and typically require a tradeoff between distance and near visual acuity in order to provide a functional range. Pharmacologic pupil modulation allows physicians to leverage the principles of small aperture optics by extending depth of focus with minimal distance vision compromise. In this scenario, presbyopia drops can further extend the range of advanced IOL technology.

A patient with a highly aberrated cornea. Higher-order aberrations are inherently pupil-dependent; as pupil diameter increases, peripheral optical irregularities negatively impact visual quality. [Oshika 2006] Accordingly, controlled reduction of pupil size can improve optical quality by limiting the functional aperture of the eye. This principle can be leveraged both when evaluating surgical candidacy and when troubleshooting suboptimal postoperative outcomes. In selected patients, pharmacologic pupil modulation offers a means of improving visual quality without further surgical intervention.

In each of these examples, pharmaceutical presbyopia therapy transforms the way we think about refractive surgery; not merely as a single-point correction, but as part of a continuum in which optics can be dynamically and safely optimized to meet visual goals. Controlling pupil size can have a significant effect on the extent of one's visual range, while simultaneously improving the quality of visual function. Integrating these pharmaceuticals allows physicians to expand the functional limits of both corneal and lens based refractive surgery.

Direct-to-Consumer Marketing and Patient Motivation

The introduction of presbyopia drops has sparked several notable direct-to-consumer marketing campaigns. Pharmaceutical companies are heavily investing in educating the public about these new options. While direct marketing sometimes creates clinical challenges, it also drives educated and highly motivated individuals directly into your practice. These patients bring specific questions and a strong desire to experience these medications, and such a paradigm shift requires your team be ready to discuss the clinical realities and appropriate expectations and empowered to help determine candidate suitability. When you proactively guide these conversations, you position yourself as a knowledgeable, innovative authority in modern eye care.

Next Steps & Call to Action

Presbyopia drops have meaningfully expanded the refractive paradigm. Historically, clinicians have had three primary options to address refractive error: spectacles, contact lenses, and refractive surgery. The emergence of pharmacological agents for refractive correction introduces a fourth option that is both noninvasive and reversible. Supported by growing safety and efficacy data, pupil modulation expands rather than replaces the tools available to modern practices. Presbyopia drops aren't just a "niche" option; rather, they maintain a unique place in our toolbox to treat the entirety of the refractive continuum. Just as contact lenses or refractive surgery may not be optimal considerations for every patient, the capabilities and limitations of presbyopia pharmaceuticals must be weighed and balanced with individual goals. Expanding our mindset to include this emerging category will help elevate comprehensive refractive care, and more importantly reach a group of patients for which we previously had limited options.

This shift in mindset begins by viewing refractive care as a spectrum rather than a hierarchy of escalating interventions. The distinction between good and great clinicians lies in their ability to individualize care, essentially tailoring treatment strategies to align with a patient's visual demands and lifestyle. Pharmaceutical therapy occupies a flexible position within this spectrum. It may serve as bridge therapy for early presbyopes, as situational or environment-specific enhancement, or as a long-term standalone strategy in appropriately selected individuals. This modality also has the capacity to expand functional limits of corneal- or lens-based refractive surgery. When refractive care is conceptualized as a continuum, the integration points become more easily identifiable.

Success with presbyopia drops mirrors that which we have already learned from contact lenses and refractive surgery – it is heavily dependent on proper patient selection. For those starting to incorporate drops into their repertoire, it is recommended to select early presbyopic patients with low-to-moderate degrees of refractive error. Just like any elective treatment, motivation is critical, as are realistic expectations. While this may not represent the "Holy Grail" of clinical practice, it does have the capacity to expand visual lifestyle and reduce dependency on reading glasses. Early presbyopes still naturally have accommodative demand. With a high crystalline lens clarity and predictable pupil function, they are most likely to experience an expanded near range with little distance compromise. Older patients will naturally have smaller pupils in mesopic conditions and a certain level of lens compromise which potentially may limit the value of these agents. However, that's not to say that individuals of a certain age should not be considered for these pharmaceuticals. As discussed, presbyopia drops are excellent bridge strategy for patients who are hesitant to proceed with cataract surgery. In pseudophakic patients, pupil modulation can expand the range of visual performance as well. Setting clear expectations, however, remains essential. Early, positive outcomes in ideal candidates will naturally pave the way for broader applications.

Traditionally, most ECPs approach presbyopia with a reactive mindset. We wait for our patients to complain, then present options expecting a certain level of compromise, e.g., switching from a single vision lens to a progressive or modifying a contact lens design. These conversations can be challenging, especially when framed around loss of function. Fortunately, presbyopia is highly predictable and well-understood. We are trained to recognize its onset, trajectory, and functional impact. Given this, a proactive strategy is not only reasonable, but more logical. By doing so, we can make meaningful lifestyle improvements earlier and before patient frustration escalates. This strategy positions presbyopia as more manageable and customizable rather than simply inevitable. Other areas of eyecare, for example myopia management, dry eye disease, and glaucoma, have all similarly evolved from reactive treatment models to proactive intervention. Pharmaceutical presbyopia therapy represents an opportunity to apply that same forward-thinking approach.

The emergence of these therapeutic agents symbolizes a natural progression in modern eye care. Clinicians should incorporate pharmaceutical options into routine presbyopia counseling rather than reserve it as a last-line consideration. Standardizing its discussion alongside traditional options will help normalize adoption and ensure appropriate candidates are not overlooked. Remaining open to innovation across clinical settings encourages continual growth and supports the ongoing elevation of comprehensive (and customizable) patient care.

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Table #1

Comparison of Select Clinical Trial Parameters and Endpoints [VUITY PI][QLOSI PI][VIZZ PI][YUVEZZI PI]

Drug compound	Clinical Trial	Age Range	Rx parameters	Post-LASIK / Pseudophakia	Lighting	1° Efficacy Endpoint	Assessment
Pilocarpine 1.25%	GEMINI 1 GEMINI 2	40 - 55	Emmetropes & non-emmetropes	LASIK only	Mesopic	≥3-line gain DCNVA s¯≥1-line loss CDVA at 3 hours post dose on Day 30	Binocular
Pilocarpine 0.4%	NEAR-1 NEAR-2	45 - 64	-4.50 D to +2.00 D & cylinder <2.00 D	No	Mesopic	≥3-line gain DCNVA s¯≥1-line loss CDVA at 1 hour post dose #1 on Day 8	Monocular
Aceclidine 1.44%	CLARITY-1 CLARITY-2	45 - 75	-4.00 D to +1.00 D MRSE & cylinder ≤2.00 D	Yes	Photopic	≥3-line gain DCNVA s¯≥1-line loss CDVA at 3 hours post dose on Day 1	Monocular
Carbachol 2.75% / Brimonidine 0.1%	BRIO 1 BRIO 2	45 – 80	Emmetropes only: ±0.50 D	Yes	Mesopic	≥3-line gain DCNVA s¯≥1-line loss CDVA at 1 hour post dose on Day 1	Binocular

CDVA = Corrected Distance Visual Acuity; **DCNVA** = Distance Corrected Near Visual Acuity; **MRSE** = Manifest Refraction Spherical Equivalent

Table #2

Comparison of Safety Measures Across All Pooled Phase 3 Studies [VUITY PI][QLOSI PI][VIZZ PI][YUVEZZI PI]

Drug compound	Pooled Clinical Trials	Headache	Eye Irritation	Eye Pain	Visual Impairment	Blurred/Dim Vision	Hyperemia
Pilocarpine 1.25%	GEMINI 1 & 2	14.9%	2.4%	4.3%	2.7%	4.5%	5.1%
Pilocarpine 0.4%	NEAR-1 & -2	6.8%	5.8%	1.9%	1.0%	3.6%	1.6%
Aceclidine 1.44%	CLARITY-1 & -2	13%	20%	**NR**	16%	**NR**	15%
Carbachol 2.75% / Brimonidine 0.1%	BRIO 1 & 2	15.6%	14.0%	6.7%	6.4%	**NR**	2.8%

NR = Not Reported

*** It is important to emphasize that all data presented is drawn from separate clinical trials with different designs, populations, and inclusion criteria. They do not establish head-to-head superiority. Nonetheless, in the absence of direct comparative trials, clinicians still must make practical prescribing choices, and tolerability differences apparent in the labels remain clinically meaningful.*