Acquired Blepharoptosis and the
Upneeq™ (oxymetazoline hydrochloride
ophthalmic solution) 0.1%

Phase 3 Clinical Trial Program

Acquired Blepharoptosis Background

• Blepharoptosis (also known as “ptosis” or “droopy eyelid”) is a common disorder of the eyelid thought to affect millions of American adults.1,2

• Blepharoptosis is characterized by unilateral or bilateral drooping of the upper eyelid and ranges in severity.

• Acquired blepharoptosis is often caused by stretching of or reduced nervous input to the muscles that raise the upper eyelid; it can occur at any time, but is most often associated with aging.3,4

• Other known risk factors for acquired blepharoptosis (either temporary or permanent) include ocular surgery (e.g., glaucoma or cataract surgery), hard contact lens wear, and underlying conditions, such as myasthenia gravis, stroke, Horner’s Syndrome, or pseudoptosis (dermatochalasis).5-10

• Left untreated, acquired blepharoptosis can impact a patient’s visual function.11-13

• The current standard of care in the U.S. consists of surgery, often reserved for severe cases (MRD1 <1 mm).10

• There is significant unmet need for non-surgical treatment options for acquired blepharoptosis.

UPNEEQ Overview

• UPNEEQ is a first-in-class pharmacologic treatment for acquired blepharoptosis.14

• The active ingredient of UPNEEQ is oxymetazoline, an alpha adrenoceptor agonist targeting a subset of adrenoreceptors in Müller’s muscle of the eyelid.14

• The muscles responsible for upper eyelid elevation are the levator palpebrae superioris, Müller’s muscle, and the frontalis muscle.4

• Müller’s muscle predominantly expresses α2-adrenergic receptors (activated by oxymetazoline), whereas the levator muscle is innervated by the Oculomotor nerve (not activated by oxymetazoline).

• It is thought that UPNEEQ, when applied to the eye, stimulates contraction of Müller’s muscle, raising the upper eyelid.14,15

• UPNEEQ is an aseptically prepared, sterile, preservative-free, clear, colorless to slightly yellow ophthalmic solution.14

*Estimated U.S. population over 50 years of age with blepharoptosis calculated as estimated number of individuals aged 50 and older (U.S. 2020 Census) multiplied by 11.5% prevalence observed in study by Sridrahan et al.12

IMPORTANT SAFETY INFORMATION

INDICATION
UPNEEQ™ (oxymetazoline hydrochloride ophthalmic solution), 0.1% is indicated for the treatment of acquired blepharoptosis in adults.

WARNINGS AND PRECAUTIONS

• Alpha-adrenergic agonists as a class may impact blood pressure. Advise UPNEEQ patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension or hypotension to seek medical care if their condition worsens.

Please see Important Safety Information continued on next page.
Please see accompanying full Prescribing Information and Patient Information.
UPNEEQ™ (oxymetazoline hydrochloride ophthalmic solution) 0.1% Phase 3 Clinical Trial Program

Efficacy Results

- UPNEEQ was evaluated for the treatment of acquired blepharoptosis in two randomized, double-masked, vehicle-controlled, parallel-group clinical efficacy trials. Efficacy was assessed with the Leicester Peripheral Field Test (LPFT) (primary) and photographic measurement of Marginal Reflex Distance 1 (MRD1). The primary efficacy endpoints were ordered in a hierarchy to compare UPNEEQ to vehicle on the mean increase from baseline (Day 1 Hour 0) in number of points seen on the top 4 rows of the LPFT in the study eye at Hour 6 on Day 1 and Hour 2 on Day 14.

- In Trial 1, a total of 140 subjects were randomized 94 patients to the UPNEEQ group and 46 patients to the vehicle group. Treatments were administered once daily to each eye for 42 days (6 weeks). The mean age of the subjects was 64 years. In Trial 2, a total of 164 subjects were randomized 109 patients to the UPNEEQ group and 55 patients to the vehicle group. Treatments were administered once daily to each eye for 42 days (6 weeks). The mean age of the subjects was 63 years.

- Figure 1 shows results for the primary efficacy endpoint in both pivotal Phase 3 efficacy studies. In both trials, each patient had a designated study eye. An increase in the number of points seen on the LPFT represents an improvement in the superior (upper) visual field. There was a statistically significant difference in mean change in the LPFT from baseline after instillation of UPNEEQ and vehicle, with significantly greater increases in the study eye of the UPNEEQ group evident at the 2-hour point and maintained at the 6-hour time point.

- MRD1 showed a positive effect with UPNEEQ treatment. Greater MRD1 increases were observed for the UPNEEQ group than the vehicle group on Day 1 through 6 hours post-dose and on Day 14 through 2 hours post-dose. In Trial 2, onset of the improvement in MRD1 began in some patients 5 minutes after UPNEEQ was administered (the earliest time point measured).

- An increase in MRD1 represents greater elevation of the upper eyelid.

Figure 1. Mean change in LPFT from baseline

![Figure 1](image-url)
Tolerability Profile

• A total of 360 subjects with acquired blepharoptosis were treated with UPNEEQ once daily in each eye for at least 6 weeks in three controlled Phase 3 clinical trials.
• These trials included 203 subjects treated with UPNEEQ for 6 weeks and 157 subjects treated with UPNEEQ for 12 weeks.
• Adverse reactions that occurred in 1-5% of subjects treated with UPNEEQ were punctate keratitis, conjunctival hyperemia, dry eye, blurred vision, instillation site pain, eye irritation and headache.

Summary

• Pivotal Phase 3 efficacy studies demonstrated that treatment with UPNEEQ once per day resulted in significant improvement in primary and secondary efficacy endpoints (LPFT and MRD1). Greater MRD1 increases were observed for the UPNEEQ group than the vehicle group on Day 1 through 6 hours post-dose and on Day 14 through 2 hours post-dose. In Trial 2, onset of the improvement in MRD1 began in some patients 5 minutes after UPNEEQ was administered (the earliest time point measured). Phase 3 clinical studies also demonstrated favorable safety and tolerability profile of UPNEEQ.

WARNINGS AND PRECAUTIONS

• Use UPNEEQ with caution in patients with cerebral or coronary insufficiency or Sjögren’s syndrome. Advise patients to seek medical care if signs and symptoms of potentiation of vascular insufficiency develop.
• UPNEEQ may increase the risk of angle closure glaucoma in patients with untreated narrow-angle glaucoma. Advise patients to seek immediate medical care if signs and symptoms of acute narrow-angle glaucoma develop.
• Patients should not touch the tip of the single patient-use container to their eye or to any surface, in order to avoid eye injury or contamination of the solution.

ADVERSE REACTIONS

• Adverse reactions that occurred in 1-5% of subjects treated with UPNEEQ were punctate keratitis, conjunctival hyperemia, dry eye, blurred vision, instillation site pain, eye irritation and headache.

DRUG INTERACTIONS

• Alpha-adrenergic agonists, as a class, may impact blood pressure. Caution in using drugs such as beta blockers, anti-hypertensives, and/or cardiac glycosides is advised. Caution should also be exercised in patients receiving alpha adrenergic receptor antagonists such as in the treatment of cardiovascular disease, or benign prostatic hypertrophy.
• Caution is advised in patients taking monoamine oxidase inhibitors which can affect the metabolism and uptake of circulating amines.

To report SUSPECTED ADVERSE REACTIONS or product complaints, contact RVL Pharmaceuticals at 1-877-482-3788. You may also report SUSPECTED ADVERSE REACTIONS to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. Please see accompanying full Prescribing Information and Patient Information.