



## PRIOR AUTHORIZATION POLICY

- POLICY:** Ophthalmology – Upneeq Prior Authorization Policy
- Upneeq® (oxymetazoline hydrochloride 0.1% ophthalmic solution – RVL Pharmaceuticals)

**REVIEW DATE:** 10/22/2025

### INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

## CIGNA NATIONAL FORMULARY COVERAGE:

### OVERVIEW

Upneeq, an alpha-adrenergic agonist, is indicated for the treatment of **acquired blepharoptosis** in adults.<sup>1</sup>

### Disease Overview

Blepharoptosis, also known as ptosis, is a common condition defined by abnormal drooping of one or both upper eyelids.<sup>2</sup> Blepharoptosis is either congenital or acquired; acquired blepharoptosis can occur at any age but it is most commonly seen in older adults. Most cases of acquired blepharoptosis are of aponeurotic type.<sup>2</sup> Aponeurotic blepharoptosis, also commonly known as involutional ptosis, may be due to stretching, dehiscence, or disinsertion of the levator aponeurosis. Less frequent causes of acquired blepharoptosis are myogenic (e.g., associated with myasthenia gravis), neurogenic (e.g., associated with third nerve palsy), traumatic (e.g., due to eyelid laceration with transection of the upper eyelid elevators or

disruption of the neural pathway), or mechanical (e.g., resulting from presence of eye mass, such as neurofibroma or hemangioma, or cicatrization secondary to inflammation or surgery). Blepharoptosis can cause significant psychosocial effects. Surgical interventions are the primary methods for management of blepharoptosis and can improve the patient's field of vision or for cosmetic reasons. Complications of surgery include bleeding, infection, undercorrection or overcorrection of the ptosis, eyelid asymmetry, granuloma formation, corneal foreign body sensation, and exposure keratopathy. Recurrent is not uncommon and some patients may require more than one surgical procedure.

## **Guidelines**

Upneeq is not addressed in guidelines. The American Academy of Ophthalmology issued a report (2011) detailing functional indications for upper eyelid ptosis and blepharoplasty surgery; various quantitative and qualitative criteria may be used to identify appropriate surgical candidates.<sup>3</sup> Surgical techniques vary and outcomes data are limited to low-level evidence (case series). Some studies have demonstrated median improvements of 13 points in the Leicester Peripheral Field Test (LPFT) score following surgical interventions.

## **POLICY STATEMENT**

Due to insufficient clinical efficacy data, **approval of Upneeq is not recommended**. Current Upneeq efficacy information is insufficient to determine if the medication demonstrates any clinically meaningful benefits.

## **CONDITIONS NOT COVERED**

- **Upneeq® (oxymetazoline hydrochloride 0.1% ophthalmic solution – RVL Pharmaceuticals) is considered to be experimental, investigational, or unproven due to insufficient data establishing safety, efficacy, and improved health outcomes for any condition, including the following, regardless of U.S. Food and Drug Administration (FDA) approval status. Criteria will be updated as new published data are available.**

- 1. Blepharoptosis.** Due to insufficient clinical efficacy data, approval of Upneeq for treatment of blepharoptosis is not recommended. Upneeq was studied in two randomized, double-masked, placebo-controlled, multicenter Phase 3 studies (published) [n = 304].<sup>1,4</sup> Patients with acquired ptosis and superior visual field deficit in at least one eye at screening were randomized 2:1 to Upneeq or vehicle. Study medication was self-administered as a single drop per eye, once daily in the morning for 42 days (6 weeks). The primary endpoint was change from baseline in number of points seen in the top four rows on the Leicester Peripheral Field test (LPFT), which assesses superior visual field deficits due to ptosis on Day 1 (6 hours after instillation) and Day 14 (2 hours after instillation). The secondary endpoint was change from baseline in marginal reflex distance 1 (MRD1), which is the distance between the center of the papillary light reflex and the upper eyelid margin with the eye in primary gaze,

on Days 1 and 14. Compared with vehicle, Upneeq provided a statistically significant incremental benefit in. FT and a significantly greater, but numerically small, change in MRD1 from baseline, it is unclear if these incremental changes (between Upneeq and vehicle) would correspond with clinically meaningful improvement. In addition, the studies were 6 weeks in duration (primary and secondary endpoints were assessed on Days 1 and 14); there are no long-term efficacy data for Upneeq for this condition. Upneeq’s role in the management of patients with blepharoptosis is not established. A pooled analysis of the two Phase 3 studies showed that onset of action of Upneeq was rapid and sustained through Day 42; largest difference between Upneeq and vehicle was observed 2 to 6 hours after administration.<sup>5</sup> A systematic review and meta-analysis noted although Upneeq is more effective than vehicle for the treatment acquired blepharoptosis, there are no studies that compare Upneeq to current treatments for belpharoptosis.<sup>6</sup>

- 2. Conjunctivitis.** Oxymetazoline solution 0.1% has not been evaluated for conjunctivitis.
- 3. Cosmetic uses.** Coverage of Upneeq for cosmetic uses (i.e., blepharoptosis when functional limitation is absent) is not recommended as cosmetic uses are excluded from coverage in a typical pharmacy benefit.

## REFERENCES

1. Upneeq® ophthalmic solution [prescribing information]. Bridgewater, NJ: RVL Pharmaceuticals; May 2023.
2. Al-Zubidi N, Plemel D, Yen MT, et. Blepharoptosis. Updated June 29, 2024. Available at: <https://eyewiki.org/Blepharoptosis#:~:text=Blepharoptosis%20is%20an%20abnormal%20low,occur%20in%20conjunction%20with%20blepharoptosis>. Accessed on October 15, 2025.
3. Cahill KV, Bradley EA, Meyer DR, et al. Functional indications for upper eyelid ptosis and blepharoplasty surgery: a report by the American Academy of Ophthalmology. *Ophthalmology*. 2011;118(12):2510-2517.
4. Slonim CB, Foster S, Jaros M, Kannarr SR, et al. Association of oxymetazoline hydrochloride, 0.1%, solution administration with visual field in acquired ptosis: a pooled analysis of 2 randomized clinical trials. *JAMA Ophthalmol*. 2020 Nov 1;138(11):1168-1175.
5. Bacharach J, Wirta DL, Smyth-Medina R, et al. Rapid and sustained eyelid elevation in acquired blepharoptosis with oxymetazoline 0.1%: randomized phase 3 trial results. *Clin Ophthalmol*. 2021 Jun 25;15:2743-2751.
6. Newland M, Eberly H, Ma C, and Lighthall JG. The use of oxymetazoline 0.1% ophthalmic solution for acquired blepharoptosis: a systematic review. *Laryngoscope*. 2025;135:8-14.

## HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	09/20/2023
Annual Revision	No criteria changes.	10/02/2024
Annual Revision	No criteria changes.	10/22/2025

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