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Oxymetazoline Ophthalmic Solution

Table of Contents

Related Coverage Resources

Overview 1
Conditions Not Covered 1
Background..... 2
References 2

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Overview

This policy addresses the usage of oxymetazoline 0.1% ophthalmic solution (Upneeq™).

Conditions Not Covered

Cosmetic uses. Coverage of oxymetazoline 0.1% ophthalmic solution (Upneeq) for cosmetic uses (i.e., blepharoptosis when functional limitation is absent) are excluded from coverage as not medically necessary.

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

- 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 III studies (published) [n = 304]. 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. Although Upneeq provided a statistically significant incremental benefit over vehicle in LPFT, the

difference between the groups was small compared with what is typically observed following surgical interventions. Significantly greater, but numerically small, changes in MRD1 from baseline were observed in the Upneeq group vs. vehicle. 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.

2. **Conjunctivitis.** Oxymetazoline solution 0.1% has not been evaluated for conjunctivitis.

Background

OVERVIEW

Upneeq, an alpha-adrenergic agonist, is indicated for the treatment of acquired blepharoptosis in adults.¹

Disease Overview and Clinical Efficacy

Blepharoptosis, also known as ptosis, is a common condition defined by abnormal drooping of one or both upper eyelids.^{2,3} Overall incidence ranges from 4.7% to 13.5% in adults. Prevalence increases with age; a United Kingdom study reported that prevalence increased from 2.4% in patients 50 to 59 years of age to 20.8% in patients ≥ 70 years of age.³ Blepharoptosis is either congenital or acquired (underlying etiology include involutional, neurogenic, myogenic, traumatic, or mechanical).^{2,3} Transient ptosis can also occur following ocular procedures (e.g., cataract surgery). The most common cause of acquired ptosis is stretching, dehiscence, or disinsertion of the levator muscle complex related to aging. Ptosis can partially or completely affect vision and it can also affect patients' appearance, which can increase levels of anxiety and depression. Surgical interventions are the standard of care and are effective in improving the visual field. However, surgery may be associated with complications and risks of asymmetry, under- or over-correction which can require surgical revision, bleeding, and infection.

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.⁴ 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.

References

1. Upneeq ophthalmic solution [prescribing information]. Bridgewater, NJ: RVL Pharmaceuticals; May 2023.
2. 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.
3. 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.
4. 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.

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