Clinical Policy: Oxymetazoline (Rhofade, Upneeq)

Reference Number: PA.CP.PMN.86
Effective Date: 04/2019
Last Review Date: 04/2024

Description
Oxymetazoline (Rhofade®) is a topical alpha-1a adrenoreceptor agonist.

Oxymetazoline ophthalmic solution (Upneeq®) is an alpha-2 adrenergic receptor agonist.

FDA Approved Indication(s)
Rhofade is indicated for the topical treatment of persistent facial erythema associated with rosacea in adults.

Upneeq is indicated for the treatment of acquired blepharoptosis in adults.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Rhofade and Upneeq are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Facial Erythema Associated with Rosacea (must meet all)**:**
1. Diagnosis of persistent facial erythema associated with rosacea;
2. Request is for Rhofade;
3. Age ≥ 18 years;
4. If papules or pustules are present, a failure of or concomitant treatment with any of the following agents, unless clinically significant adverse effects are experienced or all are contraindicated: topical metronidazole, oral doxycycline, ivermectin cream, Finacea;
5. Dose does not exceed 30 mg (1 tube) per month.

Approval duration: 12 months

B. Acquired Blepharoptosis (must meet all)**:**
1. Diagnosis of acquired blepharoptosis/ptosis (e.g., aponeurotic, neurologic ptosis);
2. Request is for Upneeq;
3. Prescribed by or in consultation with an optometrist or ophthalmologist;
4. Age ≥ 13 years;
5. Member does not have congenital or mechanical ptosis;
6. Documentation of baseline visual peripheral field test (e.g., Leicester peripheral field test [LPFT]) demonstrating visual field loss;
7. Documentation of baseline marginal reflex distance 1 (MRD-1) ≤ 2 mm;
8. Dose does not exceed 1 carton (30 single use containers) per affected eye per month.

Approval duration: 12 months

C. Other diagnoses/indications:
1. Refer to the off-label use if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. Facial Erythema Associated with Rosacea (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Request is for Rhofade;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed 30 mg (1 tube) per month.

Approval duration: 12 months

B. Acquired Blepharoptosis (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Reqeust is for Upneeq;
3. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in visual peripheral field test (e.g., LPFT) or MRD-1;
4. Dose does not exceed 1 carton (30 single use containers) per affected eye per month.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
LPFT: Leicester peripheral field test
MRD: marginal reflex distance

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
metronidazole (Metrocream® 0.75%, Metrogel® 1%, Metrolotion® 0.75%)	**Rosacea** Apply thin film topically to affected area QD for 1% and BID for 0.75%	No maximum dosage information is available
azelaic acid 15% gel (Finacea®)	**Rosacea** Apply in a thin film topically to the affected area BID Reassess if no improvement in 12 weeks.	No maximum dosage information is available
doxycycline (Oracea)®	**Rosacea** Lesions (papules and pustules): 40 mg PO once daily in the morning (1 hour before or 2 hours after a meal)	300 mg/day; 40 mg/day for Oracea
ivermectin cream 1% (Soolantra®)	**Rosacea** Apply a pea-size amount to the affected areas of the face (forehead, chin, nose, each cheek) once daily. Spread as a thin layer, avoiding the eyes and lips.	4 oz/topical application

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- None reported

Appending D: General Information

- Tetracycline agents, including doxycycline and minocycline exhibit anti-inflammatory activities at doses < 50 mg. Anti-inflammatory dose doxycycline does not exert antibiotic selection pressure and thus does not induce antibiotic resistance; its mechanism of action in rosacea appears to relate to the anti-inflammatory and biological activities of doxycycline.
- The Phase 3 clinical trials of Upneeq excluded patients with congential ptosis and mechanical ptosis (e.g., ptosis due to excess weight on the upper lid possibly from infections, inflammation, and eyelid tumors).

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Oxymetazoline cream (Rhofade)	Facial erythema associated with rosacea	Apply a pea-size amount topically QD to each of the five areas of the face (forehead, chin, nose, each cheek) avoiding the eyes and lips.	One application/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
Oxymetazoline ophthalmic solution (Upneeq)	Blepharoptosis	Instill one drop into one or both ptotic eye(s) once daily.	One drop/eye/day

VI. Product Availability

Drug Name	Availability
Oxymetazoline cream (Rhofade)	Cream, 1%: 30 g tube or pump, 60 g tube or pump
Oxymetazoline ophthalmic solution (Upneeq)	Ophthalmic solution, 0.1%: 0.3 mL (carton of 30 single patient use containers)

VII. References

1. Rhofade Prescribing Information. Irvine, CA: Allergan; November 2019. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=e82b5788-a855-4165-a81f-7f15cb874612. Accessed Accessed January 12, 2024.
2. Upneeq Prescribing Information. Bridgewater, NJ: RVL Pharmaceuticals, Inc.; July 2022. Available at: https://ecp.upneeq.com/wp-content/uploads/2022/10/Upneeq-PI-IFU.pdf. Accessed January 12, 2023.
3. Thiboutot D, Anderson R, Cook-Bolden F, et al. Standard management options for rosacea: the 2019 update by the National Rosacea Society expert committee. *J Am Acad Dermatol*. 2020; 82(6): 1501-1510. doi: 10.1016/j.jaad.2020.01.077.
4. Shaller M, Almeida LMC, Bewley A, et al. Recommendations for rosacea diagnosis, classification and management: update from the global Rosacea Consensus 2019 panel. *Br J Dermatol.* 2020; 182:1090-1091. doi: 10.1111/bjd.18420.
5. Hampton PJ, Berth-Jones J, Duarte Williamson CE, et al. British Association of Dermatologists' Clinical Standards Unit. British Association of Dermatologists guidelines for the management of people with rosacea 2021. Br J Dermatol. 2021 Oct;185(4):725-735. doi: 10.1111/bjd.20485.
6. Slonim CB, Foster S, Jaros M, 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;138:1168–75.
7. Bacharach J, Lee WW, Harrison A, et al. A review of acquired blepharoptosis: prevalence, diagnosis, and current treatment options. Eye 2021. https://doi.org/10.1038/s41433-021-01547-5.

Reviews, Revisions, and Approvals	Date
Policy created	04/2019
2Q 2020 annual review: references reviewed and updated	04/2020
Added Upneeq to policy with new criteria for blepharoptosis.	07/2020
2Q 2021 annual review: added ivermectin 1% cream as an option for failure; references reviewed and updated.	04/2021
2Q 2022 annual review: added 60 g tube and 30 and 60 g pump formulations of Rhofade; references reviewed and updated.	04/2022
2Q 2023 annual review: no significant changes; references reviewed and updated.	04/2023

Reviews, Revisions, and Approvals	Date
2Q 2024 annual review: no significant changes; references reviewed and updated.	04/2024