Clinical Policy: Oxymetazoline (Rhofade, Upneeq)

Reference Number: CP.PMN.86
Effective Date: 06.01.19
Last Review Date: 05.23
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Oxymetazoline cream (Rhofade™) is an 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 health plans affiliated with Centene Corporation® 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, 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 both of the following (a and b):
   a. 30 mg per month;
   b. 1 tube per month.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

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 both of the following (a and b):
   a. 1 carton per affected eye per month;
   b. 30 single use containers per affected eye per month.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Facial Erythema Associated with Rosacea (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
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 both of the following (a and b):
   a. 30 mg per month;
   b. 1 tube per month.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Acquired Blepharoptosis (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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 both of the following (a and b):
   a. 1 carton per affected eye per month;
   b. 30 single use containers per affected eye per month.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, 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 for all relevant lines of business 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

Appendix 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,	One application/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
		each cheek) avoiding the eyes and lips.	
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 2018. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=8968299e-2a4f-41a8-9088-6343ea6c91f4. Accessed February 7, 2023.
2. Upneeq Prescribing Information. Bridgewater, NJ: RVL Pharmaceuticals, Inc.; July 2022. Available at: https://g290de.a2cdn1.secureserver.net/wp-content/uploads/2022/10/Upneeq-PI.pdf. Accessed February 7, 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. Accessed February 7, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2019 annual review: policy split from CP.PMN.86 Brimonidine (Mirvaso), Oxymetazoline (Rhofade) into individual drug policies; added age limit; references reviewed and updated.	02.05.19	05.19
2Q 2020 annual review: no significant changes; references reviewed and updated	02.07.20	05.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
RT2: added Upneeq to policy with new criteria set for blepharoptosis; added HIM line of business.	07.27.20	11.20
2Q 2021 annual review: added ivermectin 1% cream as an option for failure; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	01.22.21	05.21
2Q 2022 annual review: no significant changes; added 60 g tube and 30 and 60 g pump formulations of Rhofade; references reviewed and updated.	01.13.22	05.22
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less.	04.27.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.10.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	02.07.23	05.23

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.