

PHARMACY COVERAGE GUIDELINE

Brimonidine

MIRVASO® (brimonidine)

RHOFADE® (oxymetazoline)

Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

Scope

- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
- The “Description” section describes the Service.
- The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
- The “Resources” section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Brimonidine generic, Mirvaso (brimonidine), Rhofade (oxymetazoline), and/or generic equivalent (if available) are considered **medically necessary** and will be approved when **ALL** of the following criteria are met:
 1. Prescriber is a physician specializing in the patient’s diagnosis or is in consultation with a Dermatologist
 2. Individual is 18 years of age or older
 3. Individual has a confirmed diagnosis of moderate to severe persistent (non-transient) facial erythema of rosacea

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4. Individual has documented failure, contraindication per FDA label, intolerance, or is not a candidate to use **TWO** of the following:
 - a. Topical azelaic acid 15%
 - b. Topical metronidazole 0.75% or 1%
 - c. Topical sodium sulfacetamide/sulfur generic 10%/5%
5. **Additional criteria for Mirvaso (brimonidine):** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for **brimonidine generic** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
6. **Additional criteria for Rhofade (oxymetazoline):** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for **brimonidine generic** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
7. **If available, additional criteria for Rhofade (oxymetazoline):** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Brimonidine generic, Mirvaso (brimonidine), Rhofade (oxymetazoline), and/or generic equivalent (if available) are considered **medically necessary** and will be approved when **ALL** of the following criteria are met (**samples are not considered for continuation of therapy**):
1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Dermatologist
 2. Individual's condition has responded while on therapy with response defined as facial erythema has improved over baseline from moderate-severe to mild using **ONE** of the following:
 - a. Patient self-assessment (PSA) describes **ONE** of the following: ([see Definitions section](#))
 - i. No redness
 - ii. Very mild redness
 - iii. Mild redness
 - b. Provider Clinical Erythema Assessment (CEA) describes **ONE** of the following: ([see Definitions section](#))
 - i. Clear skin with no erythema
 - ii. Almost clear with slight erythema
 - iii. Mild erythema with definite redness
 3. Individual has been adherent with the medication

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4. **Additional criteria for Mirvaso (brimonidine):** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for **brimonidine generic** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
 5. **If available, additional criteria for Rhofade (oxymetazoline):** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:
1. **Off-Label Use of Non-Cancer Medications**
 2. **Off-Label Use of Cancer Medications**

Description:

Brimonidine (brand Mirvaso and generic) topical gel is indicated for the topical treatment of moderate to severe persistent (non-transient) facial erythema of rosacea in adults. Brimonidine is a relatively selective alpha-2 adrenergic agonist, topical application of the gel may reduce erythema through direct vasoconstriction.

Rhofade (oxymetazoline) is an alpha1A adrenoceptor agonist indicated for the topical treatment of persistent facial erythema associated with rosacea in adults. Oxymetazoline acts as a vasoconstrictor.

Rosacea is a chronic facial dermatologic disorder that is characterized by intermittent periods of exacerbation and remission. The condition primarily affects the center of the face including the cheeks, nose, chin, and central forehead. Ocular manifestations may also be present.

Clinical signs of rosacea include central facial erythema, coarseness of the skin, inflammatory lesions (papules and pustules resembling acne), and telangiectasias. Rosacea is distinguished from acne vulgaris by the absence of comedones and by its confinement to flush areas.

The underlying cause of rosacea is unknown. Major pathogenic components appear to include chronic inflammatory, vascular changes, hormonal, and neural processes.

There are 4 subtypes of rosacea: erythematotelangiectatic, papulopustular, phymatous, ocular. The most common clinical presentations of rosacea include erythematotelangiectatic and the inflammatory (papulopustular) subtypes. Features of both subtypes are primarily localized on the central face. Persistent facial redness, recurrent facial flushing, telangiectasias, skin dryness and sensitivity are common features of erythematotelangiectatic rosacea. Lesions of papulopustular rosacea closely resemble inflammatory acne.

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The less common phymatous form of rosacea may demonstrate marked skin thickening and distortion of facial contours, there may be severe disfigurement as a result. Other areas such as the chin, cheeks, and ears may also be affected.

Ocular rosacea is not uncommon in patients with cutaneous rosacea. Clinical presentations of ocular rosacea include conjunctivitis, blepharitis, stye formation and keratitis.

Facial redness is a common cutaneous finding that may occur as a normal feature or as a consequence of cutaneous or systemic disorders. Examples of conditions that may lead to facial redness include inflammatory skin disease, photosensitive disorders, autoimmune disorders, vascular reactions, and infections.

Topical metronidazole is effective for the treatment of inflammatory papules and pustules but may also contribute to improvement in facial erythema. Similar to metronidazole, azelaic acid improves papular and pustular lesions, and may also reduce erythema. The efficacy of sulfacetamide-sulfur is limited, but a vehicle-controlled trial and an open-label study reported benefit of this agent for inflammatory lesions and erythema. Topical application of alpha agonists (brimonidine and oxymetazoline) has shown efficacy for persistent facial erythema in rosacea. Oral tetracyclines are useful for improving inflammatory papules and pustules and may reduce erythema.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
[MedWatch Forms for FDA Safety Reporting | FDA](#)

Rosacea subtypes and variants and their characteristics	
Sub-type	Characteristics
Erythematotelangiectatic	Flushing and persistent central facial erythema with or without telangiectasia
Papulopustular	Persistent central facial erythema with transient, central facial papules or pustules or both, may resemble acne vulgaris but it is without comedones, facial edema may be present
Phymatous	Thickening skin, irregular surface nodules may occur on the nose, chin, forehead, cheeks, or ears, rhinophyma is present
Ocular	Foreign body sensation in the eye, burning or stinging, dryness, itching, ocular photosensitivity, blurred vision, telangiectasia of the sclera or other parts of the eye, or periorbital edema
Variants	
Granulomatous	Non-inflammatory; hard; brown, yellow, or red cutaneous papules; or nodules of uniform size
Rosacea fulminans	Sudden appearance of papules, pustules, and nodules, along with fluctuating and draining sinuses that may be interconnecting

Score	Clinical Erythema Assessment (CEA)	Patient Self-Assessment (PSA)
0 = Clear	Clear skin with no signs of erythema	No redness
1 = Almost clear	Almost clear, slight redness	Very mild redness

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2 = Mild	Mild erythema, definite redness	Mild redness
3 = Moderate	Moderate erythema, marked redness	Moderate redness
4 = Severe	Severe erythema, fiery redness	Severe redness
Fowler L, Jarratt M, Moore A, et al.: Once daily topical brimonidine tartrate gel 0.05% is a novel treatment for moderate to severe facial erythema of rosacea: results of two multicenter, randomized and vehicle controlled studies. Br J Derm 2012; 166 (3)633-641		

Distinguishing acne vulgaris from rosacea

Acne vulgaris – patient may exhibit some or all features	Rosacea – patient may exhibit some or all features
Erythema and telangiectasias may be subtle in highly pigmented skin Acne vulgaris and rosacea can coexist in the same patient	
Most prevalent in adolescents and young adults	Most prevalent in adults 30 years of age or older
Variable distribution on face	Centrofacial distribution (cheeks, nose, chin)
Frequent shoulder chest, and/or back involvement	Ocular involvement (eye irritation, eyelid erythema, conjunctival injection, crusting, recurrent hordeolum or chalazion)
Closed comedones	Centrofacial erythema
Open comedones	Telangiectasia
Inflamed papules, pustules, or nodules	Inflamed papules and pustules
Sequelae of post-inflammatory hyperpigmentation, post-inflammatory erythema, and scarring	Sensitive skin (burning or stinging sensations)
Association with hyperandrogenic disorders (i.e., polycystic ovarian syndrome, menstrual irregularities, hirsutism, virilization)	Flushing

Resources:

Mirvaso (brimonidine) 0.33% gel product information, revised by Gladerma Laboratories LP 12-2022. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed August 26, 2024.

Brimonidine 0.33% gel product information, revised by Padagis Israel Pharmaceuticals 06-2022. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed September 29, 2024.

Rhofade (oxymetazoline) 1% cream product information, revised by Aclaris Therapeutics, Inc. 11-2018. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed August 26, 2024.

Maier LE. Management of rosacea. In: UpToDate, Owen C, Ofori AO (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through August 2024. Topic last updated June 29, 2022. Accessed September 29, 2024.

Maier LE, Helfrich YR. Rosacea: Pathogenesis, clinical features, and diagnosis. In: UpToDate, Dellavalle RP, Owen C, Ofori AO (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through August 2024. Topic last updated March 17, 2022. Accessed September 29, 2024.



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Gallo RL, Granstein RD, Kang S, et al.: Standard classification and pathophysiology of rosacea: The 2017 update by the National Rosacea Society Expert Committee. J Am Acad Dermatol 2018; 78 (1):148-195. Available at: <http://dx.doi.org/10.1016/j.jaad.2017.08.037>. Accessed October 19, 2023. Re-evaluated September 29, 2024.

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