Mirvaso® (brimonidine tartrate) external gel

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member’s specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as “Description” defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as “Criteria” defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms “experimental” and “investigational” are considered to be interchangeable.

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Description:

Mirvaso (brimonidine) topical gel is indicated for the topical treatment of moderate to severe persistent (non-transient) facial erythema of rosacea in adults.

Rosacea is a chronic facial dermatologic disorder that is characterized by intermittent periods of exacerbation and remission. Clinical signs of rosacea include central facial erythema, coarseness of the skin, inflammatory lesions (papules and pustules) resembling acne, and telangiectasias. The condition primarily affects the center of the face including the cheeks, nose, chin and central forehead. Ocular manifestations may also be present. 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, and ocular. The most common clinical presentations of cutaneous rosacea include the inflammatory (papulopustular) and erythematotelangiectatic subtypes. Other presentations include phymatous rosacea (such as rhinophyma) and
granulomatous rosacea. Ocular rosacea is not uncommon in patients with cutaneous rosacea; clinical presentations of ocular rosacea include conjunctivitis, blepharitis, stye formation and keratitis.

Brimonidine is a relatively selective alpha-2 adrenergic agonist, topical application of the gel may reduce erythema through direct vasoconstriction.

**Definitions:**

<table>
<thead>
<tr>
<th>Rosacea subtypes and variants and their characteristics</th>
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<tbody>
<tr>
<td><strong>Sub-type</strong></td>
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<tr>
<td>Erythematotelangiectatic</td>
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<tr>
<td>Papulopustular</td>
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<tr>
<td>Phymatous</td>
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<tr>
<td>Ocular</td>
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<tr>
<td><strong>Variants</strong></td>
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<tr>
<td>Granulomatous</td>
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<td>Rosacea fulminans</td>
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**Drug related events:**

**Ineffective / failure**
Use of a drug employing optimal doses (FDA-recommended doses) for optimal duration; where the condition being treated has not improved or worsened

A request for branded agent due to generic drug failure or ineffectiveness will be assessed for potential approval with documentation of use of optimal dose / duration of the generic product and meeting other criteria within the coverage guideline. When the drug in question is a combination product, there must be documentation of failure / ineffectiveness of concurrent use (each ingredient used at the same time) of individual generic components. When the drug in question is a low dose formulation, there must be documentation of failure / ineffectiveness of low dose generic formulation.

**Adverse Drug Event:** Allergic reaction / Hypersensitivity / Intolerance
Use of a drug produced a significant reaction where continued use of the drug places the individual at risk for either lack of improvement or worsening of the condition being treated or at risk for harm and the concern is documented in medical record. A significant adverse drug event is when an individual's outcome is death, life-threatening, hospitalization (initial or prolonged), disability resulting in a significant, persistent, or
permanent change, impairment, damage or disruption in the individuals' body function/structure, physical activities or quality of life, or requires intervention to prevent permanent impairment or damage.

Allergic reaction / hypersensitivity – may or may not involve the active ingredient. When the active ingredient is involved, use of same or a chemically similar agent places the individual at risk for harm when the same or chemically similar agent is used. The subsequent reaction may be the same as the original reaction or a more exaggerated response may be seen, potentially placing the individual at even greater risk for harm.

If the reaction occurred from the active/main generic ingredient; request for branded agent with same active ingredient will not be considered unless it is proven (documented) that active ingredient did not cause reaction and the request meets other criteria within the coverage guideline

Intolerance – these events represent circumstance(s) where use of a drug produced a significant reaction and continued use may result in non-adherence to proposed therapy and this concern is documented in medical record

Contraindication
Use of a drug that is not recommended by the manufacturer or FDA labelling

Use of any drug in the face of a contraindication is outside of the FDA and manufacturer's labelled recommendation and is considered investigational or experimental

Non-adherence
Individual does not follow prescribe regimen that places the individual at risk for lack of improvement or worsening of the condition being treated and this concern is documented in medical record

**Precertification:**

Precertification (Prior Authorization) is required for members with a Blue Cross Blue Shield of Arizona (BCBSAZ) pharmacy benefit for medication(s) or product(s) indicated in this guideline.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy).

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.
Criteria:

See “Resources” section for FDA-approved dosage.

- Precertification for Mirvaso (brimonidine tartrate) requires completion of the specific request form in its entirety. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. Incomplete forms will be returned.

- FDA-approved product labeling (indication, age, dosage, testing, contraindications, exclusions, etc.) of Mirvaso (brimonidine tartrate) is considered medically necessary when ALL of the following criteria are met:
  1. Individual is 18 years of age or older
  2. Medical record documentation of a confirmed diagnosis of moderate to severe persistent (non-transient) facial erythema of rosacea
  3. Medical record documentation that the individual is unable to use ALL of the following due to a failed response, significant adverse drug event or contraindication:
     - Doxycycline generic 20 mg tablet
     - Doxycycline generic 50 mg tablet or capsule
     - Finacea (azelaic acid) 15% external gel
     - Rosadan (metronidazole) 0.75% external gel
     - Metronidazole generic 0.75 % external cream, gel and lotion
     - Noritate (metronidazole) 1% external cream
     - Sodium sulfacetamide/sulfur generic 10%/5% lotion, cream
  4. Absence of ALL of the following contraindications:
     - Known hypersensitivity to any component of Mirvaso topical gel
  5. Absence of ALL of the following exclusions:
     - Application to irritated skin
     - Application to open wounds
     - Use following any laser procedure

- Mirvaso (brimonidine tartrate) for all other indications not previously listed is considered experimental or investigational based upon:
  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

This includes but is not limited to the following:
- Use in Phymatous rosacea
MIRVASO® (brimonidine tartrate) external gel (cont.)

- Use in Ocular rosacea
- Use in granulomatous rosacea
- Use in rosacea fulminans

Resources:

FDA-approved indication and dosage:

<table>
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<tr>
<th>Indication</th>
<th>Recommended Dose</th>
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| Mirvaso (brimonidine) topical gel, 0.33% is an alpha adrenergic agonist indicated for the topical treatment of persistent (nontransient) facial erythema of rosacea in adults 18 years of age or older. | • Apply a pea-sized amount once daily to each of the five areas of the face (forehead, chin, nose, each cheek) avoiding the eyes and lips.  
  • Hands should be washed immediately after applying Mirvaso topical gel.  
  • For topical use only.  
  • Not for oral, ophthalmic, or intravaginal use. |