Topical Rosacea Products

Policy # 00568
Original Effective Date: 06/21/2017
Current Effective Date: 01/01/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Rhofade™‡ (oxymetazoline) or Noritate®‡ (metronidazole) to be **eligible for coverage**** when the patient selection criteria are met for the requested drug.

Patient Selection Criteria

Coverage eligibility for Rhofade (oxymetazoline) or Noritate (metronidazole) will be considered when the following criteria are met for the requested drug:

- For Rhofade requests:
    - Patient has a diagnosis of persistent facial erythema associated with rosacea; AND
    - Patient is 18 years of age or older; AND
    - Patient has tried and failed (e.g., intolerance or inadequate response) GENERIC topical metronidazole (only if papulopustular), unless there is clinical evidence or patient history that suggests the use of GENERIC topical metronidazole (only if papulopustular) will be ineffective or cause an adverse reaction to the patient; AND
      *(Note: This criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
    - Patient has tried and failed (e.g., intolerance or inadequate response) Mirvaso®‡ (brimonidine) unless there is clinical evidence or patient history that suggests the use of Mirvaso (brimonidine) will be ineffective or cause an adverse reaction to the patient
      *(Note: This criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- For Noritate requests:
  - Patient has a diagnosis of inflammatory lesions of rosacea and BOTH of the following:
    - Patient has tried and failed (e.g., intolerance or inadequate response) TWO GENERIC topical metronidazole 0.75% or 1% agents (i.e. metronidazole 0.75% cream, gel, lotion; rosadan 0.75% cream or gel; metronidazole 1% gel) unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
    - Patient has tried and failed (e.g., intolerance or inadequate response) GENERIC azelaic acid 15% gel OR Finacea®‡ (azelaic acid) foam unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; OR

    *(Note: These criteria are additional Company requirements for coverage eligibility and will be denied as not medically necessary** if not met.)*
  - Patient has a diagnosis of erythema of rosacea and BOTH of the following:
    - Patient has tried and failed (e.g., intolerance or inadequate response) TWO GENERIC topical metronidazole 0.75% or 1% agents (i.e. metronidazole 0.75% cream, gel, lotion; rosadan 0.75% cream or gel; metronidazole 1% gel) unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
    - Patient has tried and failed (e.g., intolerance or inadequate response) Mirvaso (brimonidine) unless there is clinical evidence or patient history that suggests the use of Mirvaso (brimonidine) will be ineffective or cause an adverse reaction to the patient.

    *(Note: These criteria are additional Company requirements for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Rhofade (oxymetazoline) when the patient has NOT tried and failed both generic topical metronidazole (only if papulopustular) AND Mirvaso (brimonidine) to be **not medically necessary.****

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Based on review of available data, the Company considers the use of Noritate (metronidazole) for the treatment of inflammatory lesions of rosacea when the patient has not tried TWO generic topical metronidazole agents AND a preferred azelaic acid product to be **not medically necessary.****

Based on review of available data, the Company considers the use of Noritate (metronidazole) for the treatment of erythema of rosacea when the patient has not tried TWO generic topical metronidazole agents AND Mirvaso (brimonidine) to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Rhofade (oxymetazoline) when the patient selection criteria are not met (EXCEPT those denoted as **not medically necessary****) to be **investigational.***

Based on review of available data, the Company considers the use of Noritate (metronidazole) for indications other than the inflammatory lesions or erythema of rosacea to be **investigational.***

Background/Overview

Both Rhofade and Noritate are topical products indicated for the treatment of rosacea. Rhofade is an alpha 1a adrenoceptor agonist specifically indicated for persistent facial erythema associated with rosacea in adults. It is available in a 1% cream that should be dosed by applying a pea-sized amount once daily in a thin layer to cover the entire face (forehead, nose, each cheek, and chin) avoiding the eyes and lips. Noritate is a cream that contains metronidazole, an antibiotic that is one of the first-line treatment options for mild to moderate papules and pustules associated with rosacea. It is specifically indicated for the treatment of both inflammatory lesions and erythema of rosacea and is supplied as a 1% cream. Noritate should be dosed by applying a thin film to the entire affected area once daily.

Rosacea is a chronic and relapsing inflammatory skin disorder that primarily involves the central face. Common clinical features include facial erythema, telangiectasias, and inflammatory papules

or pustules. Treatment is often targeted to the symptom, with some agents used to manage the erythema of rosacea and others that are used for managing the inflammatory lesions. The two pharmacologic treatment options specifically used for the treatment of erythema associated with rosacea are Rhofade and Mirvaso. Because, there are currently no head to head studies between the two, no superiority claims can be made. The topical antibiotic, metronidazole, is often used to manage the inflammatory lesions and is available in numerous generic formulations (e.g., creams, gels, and lotions of various strengths). Metronidazole may also have benefit in the reduction of facial erythema. Noritate is a branded version of metronidazole cream that has not been compared directly to any of the other formulations. Generically available formulations therefore most likely represent a more cost-effective and equally clinically effective option.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Rhofade is indicated for the topical treatment of persistent facial erythema associated with rosacea in adults.

Noritate is indicated for the topical treatment of inflammatory lesions and erythema of rosacea.

Rationale/Source

The efficacy of Rhofade was established in two identical vehicle-controlled trials. In the first trial, the proportion of patients achieving the primary endpoint at day 29 was statistically significant in the Rhofade group versus the vehicle group. The results of the assessments at the following time points were: hour 3 (11.9% vs. 5.5%), hour 6 (15.5% vs. 8.3%), hour 9 (17.7% vs. 6.0%), and hour 12 (14.8% vs. 6.0%). The same can be said about trial 2 with the following results: hour 3 (14.3% vs. 7.4%), hour 6 (13.4% vs. 4.8%), hour 9 (15.5% vs. 8.5%), and hour 12 (12.3% vs. 6.1%). Longer term data showed continued efficacy over 52 weeks.

The patient selection criteria presented in this policy take into consideration the FDA approved indication of these drugs as well as other therapeutic alternatives that currently exist for this condition. There have been no direct, head to head comparisons of Rhofade to other drugs in this treatment category (e.g. Mirvaso) that would indicate Rhofade is more efficacious than any of the existing treatment modalities. Additionally, Noritate is a 1% cream formulation of metronidazole. Topical metronidazole is available in many lower cost generic formulations including metronidazole

0.75% cream, gel, and lotion; rosadan 0.75% cream and gel; and metronidazole 1% gel. The patient selection criteria presented in this policy take into consideration clinical evidence or patient history that suggests generic alternatives will be ineffective or cause an adverse reaction to the patient. Based on a review of the data, in the absence of such clinical evidence or patient history, there is no advantage of using Noritate prior to the generic alternatives.

References

1. Rhofade Drug Evaluation. Express Scripts. Updated March 2017.
2. Rhofade [package insert]. Allergan. Irvine, California. Updated January 2017.
3. Mirvaso [package insert]. Galderma Laboratories. Fort Worth, Texas. Updated August 2013.
4. Noritate [package insert]. Bausch Health US, LLC. Bridgewater, NJ. Updated June 2020.
5. Management of rosacea. UpToDate. Updated February 2020.

Policy History

Original Effective Date: 06/21/2017
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06/01/2017	Medical Policy Committee review
06/21/2017	Medical Policy Implementation Committee approval. New policy.
06/07/2018	Medical Policy Committee review
06/20/2018	Medical Policy Implementation Committee approval. No change to coverage.
06/06/2019	Medical Policy Committee review
06/19/2019	Medical Policy Implementation Committee approval. No change to coverage.
06/04/2020	Medical Policy Committee review
06/10/2020	Medical Policy Implementation Committee approval. No change to coverage.
10/01/2020	Medical Policy Committee review
10/07/2020	Medical Policy Implementation Committee approval. Changed title from "Rhofade (oxymetazoline)" to "Topical Rosacea Products." Added Noritate to the policy with criteria and background information.

Next Scheduled Review Date: 10/2021

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into

standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.