LOUISIANA BLUE

Topical Treatments for Dry Eye Disease

Policy # 00640
Original Effective Date: 01/01/2019
Current Effective Date: 01/01/2027

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.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

When Services May Be Eligible for Coverage

Based on review of available data, the Company may consider Restasis®‡ (cyclosporine ophthalmic emulsion), Restasis Multidose™‡ (cyclosporine ophthalmic emulsion), Cequa™‡ (cyclosporine ophthalmic solution), Tryptyr®‡ (acoltremon ophthalmic solution), and Vevye®‡ (cyclosporine ophthalmic solution) to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for Restasis (cyclosporine ophthalmic emulsion), Restasis Multidose (cyclosporine ophthalmic emulsion), Cequa (cyclosporine ophthalmic solution), Tryptyr (acoltremon ophthalmic solution), and Vevye (cyclosporine ophthalmic solution) will be considered when the following criteria are met for the requested drug:

- Requested drug is **Restasis, Restasis Multidose, or Cequa**:
  - Requested drug will NOT be used in combination with Xiidra®‡ (lifitegrast ophthalmic); AND
  - Patient has ONE of the following conditions:
    - Dry eye condition due to ocular inflammation associated with keratoconjunctivitis sicca (KCS); OR
    - Dry eye condition due to systemic inflammatory diseases (e.g., Sjögren syndrome, rheumatoid arthritis [RA], systemic lupus erythematosus [SLE]); OR
    - Dry eye condition due to ocular surface diseases (e.g., ocular rosacea, atopic keratoconjunctivitis, acute corneal graft rejection, blepharitis, herpetic stromal keratitis, conjunctival graft versus host disease [GVHD]); AND
  - Patient has tried and failed (e.g. intolerance or inadequate response) Xiidra after at least 3 months of therapy, Tyrvaya™‡ (varenicline nasal spray), or Miebo™‡ (perfluorohexyloctane ophthalmic solution) unless there is clinical evidence or patient history that suggests the use of Xiidra, Tyrvaya, or Miebo will be ineffective or cause an adverse reaction to the patient; AND
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

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  - Patient has tried and failed (e.g. intolerance or inadequate response) generic cyclosporine ophthalmic emulsion unless there is clinical evidence or patient history that suggests the use of generic cyclosporine ophthalmic emulsion will be ineffective or cause an adverse reaction to the patient.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Requested drug is **Tryptyr**:
  - Patient has a diagnosis of symptomatic dry eye disease; AND
  - Patient is greater than or equal to 18 years of age; AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) Xiidra after at least 3 months of therapy, generic cyclosporine ophthalmic emulsion, Tyrvaya (varenicline nasal spray), or Miebo (perfluorohexyloctane ophthalmic solution) unless there is clinical evidence or patient history that suggests the use of Xiidra, generic cyclosporine ophthalmic emulsion, Tyrvaya, or Miebo will be ineffective or cause an adverse reaction to the patient.
    *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Requested drug is **Vevye**:
  - Patient has a diagnosis of dry eye disease; AND
  - Requested drug will NOT be used in combination with Xiidra (lifitegrast ophthalmic); AND
  - Patient has tried and failed (e.g., intolerance or inadequate response) Xiidra after at least 3 months of therapy, Tyrvaya (varenicline nasal spray), or Miebo (perfluorohexyloctane ophthalmic solution) unless there is clinical evidence or patient history that suggests the use of Xiidra, Tyrvaya, or Miebo will be ineffective or cause an adverse reaction to the patient; AND
    *(Note: This specific patient selection 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) generic cyclosporine ophthalmic emulsion unless there is clinical evidence or patient history that suggests the use of generic cyclosporine ophthalmic emulsion will be ineffective or cause an adverse reaction to the patient.
    *(Note: This specific patient selection criterion is an additional Company requirement 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 Restasis (cyclosporine ophthalmic emulsion), Restasis Multidose (cyclosporine ophthalmic emulsion), Cequa (cyclosporine ophthalmic solution), Tryptyr (acoltremon ophthalmic solution), or Vevye (cyclosporine ophthalmic solution) when the patient has not tried and failed Xiidra after at least 3 months of therapy, generic cyclosporine ophthalmic emulsion, Tyrvaya, or Miebo 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 Restasis (cyclosporine ophthalmic emulsion), Restasis Multidose (cyclosporine ophthalmic emulsion), Cequa (cyclosporine ophthalmic solution), Tryptyr (acoltremon ophthalmic solution), or Vevye (cyclosporine ophthalmic solution) when the patient selection criteria are not met (other than those considered to be **not medically necessary****) to be **investigational.***

Background/Overview

The Restasis products (brand Restasis, generic cyclosporine ophthalmic emulsion, and Restasis Multidose) and Cequa contain the active ingredient, cyclosporine, and are indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. Cequa is a novel formulation of cyclosporine in which the hydrophobic cyclosporine molecules are encased in nanomicelles to facilitate the crossing of the corneal barrier. However, no head to head studies have been conducted to establish any benefit of Cequa over Restasis. In pivotal studies of Restasis, increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs. Both Restasis and Cequa are dosed one drop twice a day in each eye (approximately 12 hours apart). Vevye is another formulation of cyclosporine that contains a different vehicle that allows the drop to spread more evenly over the eye and may be better tolerated. It is indicated for the treatment of dry eye disease and also has not been compared to any other active treatment for the condition.

Tryptyr is a first in class transient receptor potential melastatin 8 (TRPM8) thermoreceptor agonist that is thought to work by increasing tear production through trigeminal nerve activation. Tryptyr contains the active ingredient, acoltremon, and is indicated for the treatment of signs and symptoms of dry eye disease. It is administered at a dose of one drop in each eye two times daily (approximately 12 hours apart). The most common adverse reaction experienced by participants in clinical trials was instillation site pain, which occurred in 50% of patients.

Even though dry eye diseases due to systemic inflammatory disease or ocular surface diseases are not technically FDA approved indications for these products, the American Academy of Ophthalmology gives recommendations for Restasis in these conditions. Other options for the treatment of dry eye diseases include Xiidra (lifitegrast ophthalmic), Miebo (perfluorohexyloctane), and artificial tears. It should be noted that patients in clinical trials of Xiidra saw an increased benefit of treatment with increased duration of use (up to 12 weeks).

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Restasis was approved in 2003 and is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca.

Cequa was approved in 2018 and is indicated to increase tear production in patients with keratoconjunctivitis sicca (dry eye).

Vevye was approved in 2023 for the treatment of the signs and symptoms of dry eye disease.

Tryptyr was approved in 2025 for the treatment of the signs and symptoms of dry eye disease.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The patient selection criteria presented in this policy take into consideration clinical evidence or patient history that suggests the alternative treatment agents for dry eye disease, Xiidra (lifitegrast ophthalmic) or Miebo (perfluorohexyloctane ophthalmic solution), are contraindicated, ineffective, or will cause an adverse reaction to the patient. Based on review of the data, if these factors are not present, there is no advantage of using the Restasis products or Cequa over Xiidra or Miebo.

The efficacy and safety of Vevye were assessed in two multicenter, randomized, studies in a total of 1369 patients with dry eye disease. In both studies, patients treated with Vevye were compared to patients treated with vehicle. At Day 29, there was a statistically significant higher percentage of eyes with increases of $\geq$ 10 mm from baseline in Schirmer's wetting. This effect was seen in approximately 10% of Vevye-treated patients versus approximately 6% of vehicle-treated patients.

The efficacy of Tryptyr for the treatment of dry eye disease was supported by results from two randomized, vehicle-controlled, Phase 3 clinical trials, COMET-2 and COMET-3, enrolling a total of 931 dry eye patients. Patients were randomized to Tryptyr or vehicle (placebo) in a 1:1 ratio and dosed twice a day for 90 days. Both trials met their primary endpoints, with 42.6% and 53.2% of patients who received Tryptyr achieving a $\geq$ 10 mm increase in Schirmer score (a measure of natural tear production) at Day 14, versus 8.2% and 14.4% of those receiving the vehicle, in COMET-2 and COMET-3, respectively.

References

1. Restasis [package insert]. Allergan. Irvine, California. Updated July 2017.
2. Xiidra [package insert]. Shire. Lexington, Massachusetts. Updated December 2017.
3. Cequa [package insert]. Sun Pharmaceutical. Cranbury, NJ. Updated August 2018.
4. Ophthalmic Dry Eye Medications Therapy Class Summary. Express Scripts. September 2018.
5. Vevye [package insert]. Harrow Eye, LLC. Nashville, TN. Updated November 2023.
6. Tryptyr [package insert]. Alcon Laboratories, Inc. Fort Worth, TX. Updated May 2025.

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10/04/2018	Medical Policy Committee review
10/17/2018	Medical Policy Implementation Committee approval. New policy.
06/06/2019	Medical Policy Committee review
06/19/2019	Medical Policy Implementation Committee approval. Added new drug, Cequa, to policy with relevant background information.
06/04/2020	Medical Policy Committee review
06/10/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/04/2020	Medical Policy Committee review
06/10/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/03/2021	Medical Policy Committee review
06/09/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/03/2022	Medical Policy Committee review
02/09/2022	Medical Policy Implementation Committee approval. Changed title from Restasis, Cequa (cyclosporine ophthalmic) to "Topical Treatments for Dry Eye Disease." Added new drug, Tyrvaya, with relevant criteria and background information.
07/07/2022	Medical Policy Committee review
07/13/2022	Medical Policy Implementation Committee approval. Added Restasis generic to policy.
07/06/2023	Medical Policy Committee review
07/12/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/02/2023	Medical Policy Committee review
11/08/2023	Medical Policy Implementation Committee approval. Added new product, Miebo, to policy with relevant criteria and background information.
04/04/2024	Medical Policy Committee review
04/10/2024	Medical Policy Implementation Committee approval. Added new product, Vevye, to policy with relevant criteria and background information.
07/02/2024	Medical Policy Committee review
07/10/2024	Medical Policy Implementation Committee approval. Removed Miebo from policy as it is no longer a targeted medication.
07/03/2025	Medical Policy Committee review
07/09/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/04/2025	Medical Policy Committee review
09/10/2025	Medical Policy Implementation Committee approval. Removed generic cyclosporine ophthalmic emulsion from the policy as a targeted product. Added generic cyclosporine ophthalmic emulsion as an option to try/fail for criteria that apply to Vevye, Tyrvaya, Restasis, Restasis Multidose, and Cequa.
12/04/2025	Medical Policy Committee review

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12/10/2025	Medical Policy Implementation Committee approval. Added new product, Tryptyr, to the policy with relevant criteria and background information.
07/21/2026	Pre Pharmacy & Therapeutics Committee review
07/22/2026	Pharmacy & Therapeutics Committee review approval. Removed Tyrvaya from the policy as a targeted medication. Added Tryvaya as a try/fail option for targeted medications. Criteria for Restasis, Restasis Multidose, Cequa, and Vevye were updated to include a criterion requiring trial and failure of generic cyclosporine.

Next Scheduled Review Date: 07/2027

*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 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.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.