BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

CEQUA® (cyclosporine) ophthalmic solution
MIEBO™ (perfluorohexyloctane) ophthalmic solution
RESTASIS® (cyclosporine) ophthalmic emulsion
TRYPTYR® (acoltremon) ophthalmic solution
TYRVAYA™ (varenicline) nasal solution
VEVYE® (cyclosporine) ophthalmic solution
XIIDRA™ (lifitegrast) ophthalmic solution
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/or 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.

Medical Necessity Requirements for TYRVAYA (varenicline spray)

Criteria for Initial Therapy:

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Prescriber Qualifications
- Prescribed by an Ophthalmologist or Optometrist or is in consultation with an Ophthalmologist or Optometrist

Indication
- Moderate to severe dry eye disease

Age Requirement
- 18 years of age or older

Baseline Clinical Evaluation
- **ONE** of the following:
  - Schirmer test
  - Tear break up time
  - Ocular surface dye staining
  - Tear film osmolarity
  - Fluorescein clearance test / tear function test

Alternative Therapies
- Failure (trial for at least three months duration), contraindication, intolerance, or not a candidate for **ALL** of the following:
  - Artificial tears
  - Generic cyclosporine 0.05 percent

Brand Specific Criteria
- **For brand Tyrvaya:** Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)

Safety
- Will not be used concurrently with other ophthalmic products for Dry Eye Disease (DED)

Additional Requirements
- Artificial tears product will be continued

Documentation Requirements
- A completed request form must be submitted including:
  - Chart notes

- Lab results
- Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualifications

- Continues to be seen by an Ophthalmologist or Optometrist or is in consultation with an Ophthalmologist or Optometrist

Clinical Response

- Positive clinical response defined as **THREE** of the following:
  - No evidence of disease progression
  - Achieved and maintains improvement in tear production over baseline
  - Achieved and maintains improvement in dry eye disease signs and symptoms over baseline
  - Achieved and maintains at least a greater than or equal to 10 mm improvement in Schirmer's Test Score

Adherence

- Adherence to medication and artificial tears product documented

Brand Specific Criteria

- **For brand Tyrvaya:** Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)

Safety

- Will not be used concurrently with other ophthalmic products for Dry Eye Disease (DED)

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement
- Lab values confirming safe use

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Continuation Therapy Criteria Approval Duration
- 12 months OR end of plan year

Medical Necessity Requirements for CEQUA (cyclosporine), MIEBO (perfluorohexyloctane), RESTASIS (cyclosporine) single-use vial or multi-dose bottle, TRYPTYR (acoltremon), VEVYE (cyclosporine), and XIIDRA (lifitegrast)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by an Ophthalmologist or Optometrist or is in consultation with an Ophthalmologist or Optometrist

Indication
- Moderate to severe dry eye disease

Age Requirement
- Restasis single use vial or multi dose bottle: 16 years or older
- Xiidra: 17 years or older
- Cequa, Miebo, Tryptyr, Vevye: 18 years or older

Baseline Clinical Evaluation
- **ONE** of the following:
  - Schirmer test
  - Tear break up time
  - Ocular surface dye staining
  - Tear film osmolarity
  - Fluorescein clearance test / tear function test

Alternative Therapies
- Failure (trial for at least three months duration), contraindication, intolerance, or is not a candidate for **BOTH** of the following:
  - Artificial tears
  - Generic cyclosporine 0.05 percent

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Generic Equivalent (if available)

Brand Specific Criteria

- **For brands Cequa, Miebo, Tryptyr, Vevye, Xiidra**: Have failure, contraindication or intolerance with **THREE** of their generic equivalents (if available) used for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)

Safety

- Will not be used concurrently with other ophthalmic products for Dry Eye Disease (DED)

Additional Requirements

- Artificial tears product will be continued

Documentation Requirements

- Completed request form including:
  - Chart notes
  - Lab results
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualifications

- Continues to be seen by an Ophthalmologist or Optometrist or is in consultation with an Ophthalmologist or Optometrist

Clinical Response

- Positive clinical response defined as **THREE** of the following:
  - No evidence of disease progression
  - Achieved and maintains improvement in tear production over baseline
  - Achieved and maintains improvement in dry eye disease signs and symptoms over baseline
  - Achieved and maintains at least a greater than or equal to 10 mm improvement in Schirmer's Test Score

Adherence

- Adherence to medication and artificial tears product documented

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Brand Specific Criteria

- **For Restasis single use vial or multi dose bottle:** Failure (trial for at least three months duration), contraindication, intolerance to **generic cyclosporine 0.05 percent**. **Note**: Failure, contraindication, or intolerance to the generic should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)
- **For brands Cequa, Miebo, Tryptyr, Vevye, Xiidra**: Have failure, contraindication or intolerance with **THREE** of their generic equivalents (if available) used for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the United States Food and Drug Administration (FDA) (see Definitions section)

Safety

- Will not be used concurrently with other ophthalmic products for Dry Eye Disease (DED)

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement
- Lab values confirming safe use

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

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:

Cequa (cyclosporine solution) 0.09% is a calcineurin inhibitor immunosuppressant indicated to increase tear production in patients with keratoconjunctivitis sicca (dry eye). Other names for dry eye include dry eye syndrome, keratoconjunctivitis sicca (KCS), and dysfunctional tear syndrome.

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Cyclosporine (as a 0.05% emulsion found in brand Restasis and generics and as a 0.1% solution found in Vevye) is a calcineurin inhibitor immunosuppressant indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca.

Miebo (perfluorohexyloctane ophthalmic solution) is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

Tyrvaya (varenicline solution) nasal spray is indicated for the treatment of the signs and symptoms of DED.

Xiidra (lifitegrast ophthalmic solution) 5% is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

Tryptyr (acoltremon) is indicated for the treatment of the signs and symptoms of DED.

Cyclosporine is an immunosuppressive agent when administered systemically. In patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca, cyclosporine emulsion is thought to act as a partial immunomodulator. The exact mechanism of action is not known.

Lifitegrast binds to the integrin lymphocyte function-associated antigen-1 (LFA-1), a cell surface protein found on leukocytes. Lifitegrast blocks the interaction of LFA-1 with intercellular adhesion molecule-1 (ICAM-1). ICAM-1 may be overexpressed in corneal and conjunctival tissues in DED. The interaction of LFA-1 and ICAM-1 can contribute to the formation of an immunological synapse resulting in T-cell activation and migration to target tissues. *In vitro* studies demonstrated that lifitegrast may inhibit T-cell adhesion to ICAM-1 in a human T-cell line and may inhibit secretion of inflammatory cytokines. The exact mechanism of action of lifitegrast in DED is not known.

The efficacy of varenicline in DED is believed to be the result of varenicline's activity at heteromeric sub-type(s) of the nicotinic acetylcholine (nACh) receptor where its binding produces agonist activity and activates the trigeminal parasympathetic pathway resulting in increased production of basal tear film. Varenicline binds with high affinity and selectivity and is a partial nACh receptor agonist of α4β2, α4α6β2, α3β4, and α3α5β4 receptors and a full α7 receptor agonist. The exact mechanism of action is unknown at this time.

Perfluorohexyloctane, a semifluorinated alkane, contains 6 perfluorinated carbon atoms and 8 hydrogenated carbon atoms. Perfluorohexyloctane forms a monolayer at the air-liquid interface of the tear film which can be expected to reduce evaporation. The exact mechanism of action for MIEBO in DED is not known.

Acoltremon, the active substance in Tryptyr, is an agonist of transient receptor potential melastatin 8 (TRPM8) thermoreceptors. TRPM8 thermoreceptor stimulation has been shown to activate trigeminal nerve signaling leading to increased basal tear production. The exact mechanism of action for TRYPTYR in dry eye disease is unknown.

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DED is a multifactorial disease of tears and ocular surface that results in ocular discomfort and visual impairment. DED can be due to ocular surface inflammation, altered tear-film composition, reduced tear production, poor lid function, environmental conditions, or diseases such as Sjögren's syndrome, meibomian gland dysfunction, or allergies. Medications such as anticholinergic drugs, antihistamines, nasal decongestants, estrogens, and many antidepressants can also cause dry eyes.

Patients may present with symptoms of chronic eye irritation associated with mild to moderate discomfort. Most patients present with symptoms of chronic eye irritation, such as eye dryness, red eyes, and burning sensation. Other common eye complaints may include general irritation, gritty sensation, foreign body sensation, excessive tearing, light sensitivity, and blurred vision.

The diagnosis of DED requires examination of the surface of the eye with a biomicroscope (also called a slit lamp). Schirmer's test quantifies tear production of each eye to determine whether the tear glands produce enough tears to keep eyes adequately moist. Results are measured in millimeters of tears collected over a five-minute time period. Wetting of less than 5 mm is indicative of deficient tear production. Ocular surface staining with fluorescein can facilitate evaluation of the tear film and demonstrate areas of damage on the ocular surface. It disperses in tear film and the longer the duration in which the dye remains evenly dispersed in the tear film, the better the quality of the tear film. The time that it takes for this tear film to “break up” or (TBUT) is an important measure of tear film integrity, a TBUT under 10 seconds is considered abnormal.

Treatment of dry eye disease is aimed at increasing or supplementing tear production, slowing tear evaporation, reducing tear resorption, or reducing ocular surface inflammation. The patient should discontinue unnecessary systemic or ocular medications that can contribute to dryness.

Artificial tears are considered first-line treatment for DED. There are several product formulations available. Preservative free forms are available for DED patients who have reactions to preservatives. Topical immune suppressants are second line and include topical cyclosporine and topical lifitegrast. Use of nasal varenicline is a newer form of delivery of medication and has a different mechanism of action that may be used if topical agents prove unsuccessful.

Definitions:

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

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Resources:

Restasis (cyclosporine) 0.05% ophthalmic emulsion product information, revised by AbbVie, Inc. 09-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 03, 2025.

Restasis Multidose (cyclosporine) 0.05% ophthalmic emulsion product information, revised by Allergan, Inc. 08-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 03, 2025.

Cequa (cyclosporine) 0.09% ophthalmic solution/drops product information, revised by Sun Pharmaceutical Industries, Inc. 07-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 03, 2025.

Vevye (cyclosporine) 0.1% ophthalmic solution/drops product information, revised by Harrow Eye, LLC. 11-2023. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 03, 2025.

Miebo (perfluorohexyloctane) ophthalmic 100% solution product information, revised by Bausch & Lomb Incorporated. 01-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 03, 2025.

Tryptyr (acoltremon) 0.003% solution product information, revised by Alcon Laboratories. 05-2025, at DailyMed http://dailymed.nlm.nih.gov. Accessed November 03, 2025.

Tyrvaya (varenicline) 0.03 mg per spray nasal spray product information, revised by Oyster Point Pharma 02-2024, at DailyMed http://dailymed.nlm.nih.gov. Accessed November 03, 2025.

Xiidra (lifitegrast) 5% ophthalmic solution/drops product information, revised by Bausch & Lomb Incorporated 12-2023, at DailyMed http://dailymed.nlm.nih.gov. Accessed November 03, 2025.

Shtein RM. Dry eye disease. In: UpToDate, Jacobs DS, Li H (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2025. Topic last updated January 05, 2026. Accessed January 26, 2026.

Baer AN, Akpek EK. Treatment of moderate to severe dry eye in Sjogren's syndrome. In: UpToDate, Fox R, Seo P (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2025. Topic last updated March 29, 2024. Accessed January 26, 2026.

Amescua G, Ahmad S, Cheung AY, et al.: Dry Eye Syndrome Preferred Practice Pattern. American Academy of Ophthalmology. Dry Eye Syndrome PPP 2023 - American Academy of Ophthalmology.Accessed January 27, 2024. Re-evaluated January 26, 2026.