

## PHARMACY COVERAGE GUIDELINE

### TYRVAYA™ (varenicline) nasal solution XIIDRA™ (lifitegrast) ophthalmic solution

---

#### **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 precertification is available at [www.azblue.com/pharmacy](http://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](mailto:Pharmacyprecert@azblue.com).

---

#### **Criteria:**

##### **TYRVAYA (varenicline)**

- **Criteria for initial therapy:** Tyrvaya (varenicline) nasal spray is 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 an Ophthalmologist or Optometrist
  2. Individual is 22 years of age or older
  3. A confirmed diagnosis of dry eye disease (DED) determined by a Schirmer Test Score (STS) of less than 5 mm at baseline

ORIGINAL EFFECTIVE DATE: 11/17/2016 | ARCHIVE DATE: | LAST REVIEW DATE: 02/17/2022 | LAST CRITERIA REVISION DATE: 08/18/2022

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

## PHARMACY COVERAGE GUIDELINE

### TYRVAYA™ (varenicline) nasal solution XIIDRA™ (lifitegrast) ophthalmic solution

---

4. Individual has failure of at least 3 months, contraindication per FDA label or intolerance to **ALL** of the following:
  - a. Artificial tears **and** Lacrisert (hydroxypropyl cellulose) insert
  - b. Generic for Restasis (cyclosporine) 0.05% **or** Cequa (cyclosporine) 0.09%
  - c. Xiidra (lifitegrast) 5%
5. Artificial tears product will be continued

**Initial approval duration:** 6 months

- **Criteria for continuation of coverage (renewal request):** Tyrvaya (varenicline) is considered **medically necessary** and will be approved when **ALL** 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 an Ophthalmologist or Optometrist
2. Individual's condition has responded while on therapy with response defined as **THREE** of the following:
  - a. No evidence of disease progression
  - b. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use
  - c. Achieved and maintains improvement in tear production over baseline
  - d. Achieved and maintains improvement in DED signs and symptoms over baseline
  - e. Achieved and maintains at least a  $\geq 10$  mm improvement in Schirmer's Test Score (STS)
3. Individual has been adherent with the medication **and** the artificial tears product

**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**
- 

### XIIDRA (lifitegrast)

- **Criteria for initial therapy:** Xiidra (lifitegrast) is 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 an Ophthalmologist or Optometrist

## PHARMACY COVERAGE GUIDELINE

### TYRVAYA™ (varenicline) nasal solution XIIDRA™ (lifitegrast) ophthalmic solution

---

2. Individual is 17 years of age or older
3. A confirmed diagnosis of dry eye disease (DED) determined by **ONE** of the following diagnostic tests:
  - a. Schirmer test (aqueous tear production and clearance)
  - b. Tear break-up time
  - c. Ocular surface dye staining
  - d. Tear film osmolarity
  - e. Fluorescein clearance test / tear function test
4. Individual has failure of at least 3 months, contraindication per FDA label or intolerance to **BOTH**:
  - a. Artificial tears **and** Lacrisert (hydroxypropyl cellulose) insert
  - b. Generic for Restasis (cyclosporine) 0.05% **or** Cequa (cyclosporine) 0.09%
5. Artificial tears product will be continued

**Initial approval duration:** 6 months

- **Criteria for continuation of coverage (renewal request):** Xiidra (lifitegrast) is 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 an Ophthalmologist or Optometrist
2. Individual's condition responded while on therapy with response defined as **THREE** of the following:
  - a. No evidence of disease progression
  - b. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use
  - c. Achieved and maintains improvement in tear production over baseline
  - d. Achieved and maintains improvement in DED signs and symptoms over baseline
  - e. Achieved and maintains at least a  $\geq 10$  mm improvement in Schirmer's Test Score (STS)
3. Individual has been adherent with the medication **and** the artificial tears product

**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**

## PHARMACY COVERAGE GUIDELINE

### TYRVAYA™ (varenicline) nasal solution XIIDRA™ (lifitegrast) ophthalmic solution

---

#### **Description:**

Xiidra (lifitegrast ophthalmic solution) 5% is indicated for the treatment of the signs and symptoms of dry eye disease (DED). Other names for dry eye include dry eye syndrome, keratoconjunctivitis sicca (KCS), and dysfunctional tear syndrome.

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

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  $\alpha 4\beta 2$ ,  $\alpha 4\alpha 6\beta 2$ ,  $\alpha 3\beta 4$ , and  $\alpha 3\alpha 5\beta 4$  receptors and a full  $\alpha 7$  receptor agonist. The exact mechanism of action is unknown at this time.

DED is a multifactorial disease of the 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

ORIGINAL EFFECTIVE DATE: 11/17/2016 | ARCHIVE DATE: | LAST REVIEW DATE: 02/17/2022 | LAST CRITERIA REVISION DATE: 08/18/2022

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

## PHARMACY COVERAGE GUIDELINE

### TYRVAYA™ (varenicline) nasal solution XIIDRA™ (lifitegrast) ophthalmic solution

---

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.

---

#### **Resources:**

Cequa (cyclosporine) 0.09% solution/drops product information, revised by Sun Pharmaceutical Industries, Inc. 01-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed November 05, 2021.

Eysuvis (loteprednol) 0.25% suspension/drops product information, revised by Kala Pharmaceuticals, Inc. 10-2020. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed November 05, 2021.

Lacrisert (hydroxypropyl cellulose) 5 mg ophthalmic insert product information, revised by Bausch & Lomb Incorporated 10-2019. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed November 05, 2021.

Restasis (cyclosporine) 0.05% emulsion product information, revised by Allergan, Inc. 07-2017. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed November 05, 2021.

Tyrvaya (varenicline) 0.03 mg nasal spray product information, revised by Oyster Point Pharma 10-2021, at DailyMed <http://dailymed.nlm.nih.gov>. Accessed November 05, 2021.

Xiidra (lifitegrast) 5% ophthalmic solution product information, revised by Novartis Pharmaceuticals Corporation 06-2020, at DailyMed <http://dailymed.nlm.nih.gov>. Accessed November 05, 2021.

Shtein RM. Dry eye disease. In: UpToDate, Jacobs DS, Givens J (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Topic last updated May 24, 2021. Accessed November 05, 2021.

Baer AN, Akpek EK. Treatment of moderate to severe dry eye in Sjogren's syndrome. In: UpToDate, Fox R, Romain PL (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Topic last updated June 16, 2020. Accessed November 05, 2021.