BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**11/17/2016**
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TYRVAYA™ (varenicline) nasal solution
XIIDRA™ (lifitegrast) ophthalmic solution

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.

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.

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.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **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 or forms without the chart notes will be returned.**

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

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

  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%

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Tyrvaya (varenicline) nasal spray is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  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
     a. Response is defined as **THREE** of the following:
        i. No evidence of disease progression
        ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use
        iii. Achieved and maintains improvement in tear production over baseline
        iv. Achieved and maintains improvement in DED signs and symptoms over baseline
        v. Achieved and maintains at least a ≥ 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

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

- 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

  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:

  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
     a. Response is defined as **THREE** of the following:
        i. No evidence of disease progression

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

ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use
iii. Achieved and maintains improvement in tear production over baseline
iv. Achieved and maintains improvement in DED signs and symptoms over baseline
v. Achieved and maintains at least a ≥ 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**

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 α4β2, α4α6β2, α3β4, and α3α5β4 receptors and a full α7 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 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) nasal solution
XIIDRA™ (lifitegrast) ophthalmic solution

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.