BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 11/17/16**
SECTION: DRUGS	**LAST REVIEW DATE: 11/16/17**
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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.**

XIIDRA™ (lifitegrast) ophthalmic solution (cont.)

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), dysfunctional tear syndrome, lacrimal keratoconjunctivitis, evaporative tear deficiency, aqueous tear deficiency, and LASIK-induced neurotrophic epitheliopathy (LNE).

Xiidra (lifitegrast ophthalmic solution) binds to the integrin lymphocyte function-associated antigen-1 (LFA-1), a cell surface protein found on leukocytes. Lifitegrast binds to LFA-1 and blocks the interaction of LFA-1 with intercellular adhesion molecule-1 (ICAM-1). ICAM-1 may be overexpressed in corneal and conjunctival tissues in dry eye disease. 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 dry eye disease is not known.

Dry eye disease (DED)

- 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

- The tear film of the eye includes aqueous, mucous, and lipid components
    - Production of tear film relies on an interaction between the lacrimal glands, eyelids, and ocular surface, which together are known as the lacrimal functional unit (LFU)
    - Dysfunction of any component in the LFU can lead to DED

- DED often classified into two general groups: decreased tear production and increased evaporative loss
    - In both groups, tear film hyperosmolarity and ocular surface inflammation make possible the variety of symptoms and signs
    - Decreased tear production:
        - The reduced volume of aqueous fluid leads to hyperosmolarity of the tear film and subsequently the ocular surface, which provokes inflammation of the ocular surface cells
    - Increased evaporative loss:
        - Excessive water loss from the ocular surface without any lacrimal dysfunction leads to tear film instability and a similar cycle of tear hyperosmolarity and LFU inflammation that is seen with decreased tear production

- Risk factors for DED include:
    - Advanced age
    - Female gender
    - Hormonal changes (primarily due to decreased androgens)
    - Systemic diseases (such as diabetes mellitus, Parkinson disease)
    - Wearing contact lenses

- Systemic medications (antihistamines, anticholinergics, estrogens, isotretinoin, selective serotonin receptor antagonists, amiodarone, nicotinic acid)
- Ocular medications (especially those containing preservatives)
- Nutritional deficiencies (such as vitamin A deficiency)
- Decreased corneal sensation
- Ophthalmic surgery (especially corneal refractive surgery)
- Low humidity environments

- Most patients will 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
    - Blurred vision

- There is no single definitive test or consensus of criteria to diagnose DED, it is diagnosed primarily on the basis of patient symptoms and supporting findings on the physical examination
  - The diagnosis of DED requires examination of the surface of the eye (ocular surface) with a biomicroscope (also called a slit lamp)
  - The eye specialist should perform a thorough slit lamp evaluation along with other tests to assess the status of the LFU to determine the severity of disease and possible etiologies

- The following tests may be performed:
  - Ocular surface staining with Fluorescein, Lissamine green or Rose Bengal which are non-toxic stains that can facilitate evaluation of the tear film and demonstrate areas of damage on the ocular surface
    - Fluorescein is used to stain for areas of discontinuity in the epithelial surface of the cornea
      - It disperses in tear film, 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
      - Fluorescein also allows detection of small areas on the cornea where the lining cells have been lost due to dryness or other forms of damage
    - Lissamine green and Rose Bengal are used to stain areas of devitalized epithelium in the cornea and conjunctiva
      - They are used to demonstrate ocular surface changes associated with insufficient tear flow and excessive dryness
  - Schirmer's test quantifies tear production of each eye to determine whether the tear glands produce enough tears to keep eyes adequately moist

        - Small strips of filter paper are placed in the lower eyelids of each eye, either with or without prior instillation of anesthetic eye drops.
        - 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
    - Tear hyperosmolarity
        - Osmolarity is measured using the hand-held device, which collects a minute quantity of tear from the ocular surface
        - The higher the osmolarity, the more severe the dry eye
        - Osmolarity values above 308 mOsms/L are indicative of dry eye disease
    - Ocular surface inflammation testing for the presence of matrix metalloproteinase 9 (MMP-9) as a marker of ocular surface inflammation
        - MMP-9 is a nonspecific inflammatory mediator that is expressed by stressed epithelial cells, and it has been shown to be elevated in dry eye disease
        - MMPs are important contributors to ocular surface destruction, corneal ulceration, and perforation
        - A positive result occurs when the concentration of MMP-9 in the sample is ≥40 ng/mL

- Treatment for 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

- Treatments for dry eye disease may include:
    - Artificial tears – are first-line treatment for DED
        - Products contain cellulose to maintain viscosity, a spreading agent such as polyethylene glycol or polyvinyl alcohol to prevent evaporation, and a preservative to prevent contamination
        - They are available without a prescription, in liquid, gel, and ointment forms
        - Preservative-free forms are used in individuals with DED who have reactions to the preservatives
        - Higher-viscosity gels and ointments are also available and can be used if patients feel that the eye drops are not providing enough symptomatic relief
        - These products generally need to be used indefinitely
        - May need 3-4 weeks to see a significant improvement
    - Topical cyclosporine 0.05% emulsion
        - Immunosuppressive agent found to be relatively safe, well-tolerated, and improves signs and symptoms of DED significantly in some populations
        - Patients with evidence of local mild inflammation on the ocular surface or a systemic condition associated with inflammation tend to have the highest likelihood of response
        - Some patients with dry eyes from surgical procedures, contact lens use, or thyroid orbitopathy may not respond
        - May need up to 6 weeks or more to see a noticeable improvement
    - Topical lifitegrast 5.0% eye drop formulation
        - Integrin antagonist that showed improvement of dry eye signs and symptoms in patients with mild to moderate and moderate to severe symptoms

Xiidra (lifitegrast)

Medication class:
Lymphocyte function-associated antigen 1 (LFA-1) antagonist

FDA-approved indication(s):
- Treatment of the signs and symptoms of dry eye disease (DED)

Recommended Dose:
- One drop of Xiidra twice daily (approximately 12 hours apart) into each eye using a single-use container. Discard the single-use container immediately after using in each eye

Maximum dosage
- Not stated

Available Dosage Forms:
- Ophthalmic solution containing lifitegrast 5% (50 mg/mL) in a foil pouch with 5 x 0.2 mL single-use containers. Carton contains 60 single-use containers or 12 pouches

Warnings and Precautions:
- Keep unused containers in foil pouch to protect from light
- Do not save any unused Xiidra, there is extra drug in each container in case placement of drops misses eye

Criteria:

- **Criteria for initial therapy:** Xiidra (lifitegrast) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Provider is an eye specialist (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:
     - Schirmer test (aqueous tear production and clearance)
     - Tear break-up time
     - Ocular surface dye staining
     - Tear film osmolarity
     - Fluorescein clearance test / tear function test

  4. Individual has failure, contraindication or intolerance to **BOTH**:
     - Artificial tears AND
     - Restasis (cyclosporine

  Initial approval duration: 12 months

XIIDRA™ (lifitegrast) ophthalmic solution (cont.)

- **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 Ophthalmologist or Optometrist

  2. Individual's condition responded while on therapy
     - Response is defined as:
       - Increased tear production or improvement in DED symptoms

  3. Individual has been adherent with the medication **and** the artificial tears product

  Renewal duration: 12 months

Resources:

Xiidra. Package Insert. Revised by manufacturer 07/2016. Accessed 9/9/16.

UpToDate: Dry eyes. Current through Sep 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/dry-eyes?source=search_result&search=dry%20eye&selectedTitle=1~150

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:		Dosage Form:
Directions for Use:	Quantity:	Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.