Ophthalmic Immunomodulators Prior Authorization with Quantity Limit Criteria

This program applies to FlexRx Open, FlexRx Closed, GenRx Open, GenRx Closed, Health Insurance Marketplace and KeyRx formularies.

This is a FlexRx standard and GenRx standard prior authorization program.

FDA APPROVED INDICATIONS AND DOSAGE[1,4,6]

Agent	Indication	Dosage and Administration
Restasis® (cyclosporine ophthalmic emulsion)	Indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs.	Instill one drop of ophthalmic emulsion twice a day in each eye approximately 12 hours apart
Xiidra™ (lifitegrast ophthalmic solution)	Treatment of the signs and symptoms of dry eye disease.	One drop twice daily in each eye (approximately 12 hours apart).

CLINICAL RATIONALE

The American Academy of Ophthalmology has categorized dry eye into three severity levels based on symptoms and signs. Because of the nature of the disease, the classifications are imprecise as the characteristics overlap between levels of severity.[2]

- Mild dry eye
  - Symptoms of irritation, itching, soreness, ocular discomfort, burning or intermittent blurred vision.
- Moderate dry eye
  - Increased discomfort and frequency of symptoms, and negative effect on visual function may become more consistent.
- Severe dry eye
  - Increasing frequency of symptoms that may become constant as well as potentially disabling visual symptoms.

The American Academy of Ophthalmology recommend treating mild dry eyes with the following:[2,5]

- Education and environmental modifications
- Elimination of offending topical or systemic medications
- Aqueous enhancement using artificial tear substitutes, gels, or ointment
- Eyelid therapy (warm compresses and eyelid scrubs)
- Treatment of contributing ocular factors such as blepharitis or meibomiantitis
- Correction of eyelid abnormality

For treatment of moderate dry eye the following are recommended in addition to mild dry eye treatment options:[2,5]

- Topical anti-inflammatory agents (topical cyclosporine and corticosteroids), systemic omega 3 fatty acids supplements

- Punctal plugs
- Spectacle side shields and moisture chambers

For treatment of severe dry eye the following are recommended in addition to mild and moderate dry eye treatment options:[2,5]

- Systemic cholinergic agonists
- Systemic anti-inflammatory agents
- Mucolytic agents
- Autologous serum tears
- Contact lenses
- Permanent punctal occlusion
- Tarsorrhaphy

Because of the inconsistent correlation between reported symptoms and clinical signs as well as the relatively poor specificity and/or sensitivity of clinical tests, patients with suggestive symptoms without signs should be placed on trial treatments with artificial tears when other potential causes of ocular irritation have been eliminated. As the severity of the dry eyes increases, aqueous enhancement of the eye using topical agents is appropriate. Emulsions, gels, and ointments can be used. The use of artificial tears may be increased, but the practicality of frequent tear instillation depends on the lifestyle or manual dexterity of the patient. Non-preserved tear substitutes are generally preferable; however, tears with preservatives may be sufficient for patients with mild dry eye and an otherwise healthy ocular surface. When tear substitutes are used frequently and chronically (e.g. more than 4 times a day), non-preserved tears are generally recommended. It is imperative to treat any causative factors that are amenable to treatment. Tear replacement is frequently unsuccessful when used as the sole treatment if additional causative factors are not concomitantly addressed.[2]

Anti-inflammatory therapies may be considered in addition to aqueous enhancement therapies. However, since dry eye symptoms tend to wax and wane over long periods of time, the lack of long-term data on the effectiveness of cyclosporine and the costs of longer-term (e.g. annual, lifetime) treatment should be weighed. It is also unclear whether the effects observed in cyclosporine ophthalmic emulsion clinical trials are clinically significant, and many subgroups of dry eye patients (e.g. those with meibomian gland dysfunction or keratoconjunctivitis sicca) are unlikely to experience the same benefit.[2]

The Sjogren's Syndrome Foundation's Clinical Practice Guidelines on Ocular Management in Sjögren Patients states the following.[3]

- Management depends upon the nature of the dry and the severity of disease.
- In early disease, tear replacement with topically applied artificial tear or lubricant solutions may be sufficient, but progressive or more severe inflammation of the lacrimal gland and ocular surface occur both as an inciting event in many cases and as a secondary effect as the dry eye disease worsens, called keratoconjunctivitis sicca (KCS), requires the use of dietary supplements (omega 3 essential fatty acids), anti-inflammatory measures (e.g., topical corticosteroids or cyclosporine), or oral secretagogues.
- Plugging of the lacrimal puncta can be done once the inflammatory component of dry eye is controlled. Control of lid margin (meibomian gland) disease may require topical antibiotic or systemic doxycycline therapy. The most severe cases of dry eye, particularly those unresponsive to more standard therapy, may require use of topical autologous serum or partial closure of the interpalpebral fissure to reduce surface exposure. Scleral contact lenses may be needed to control severe ocular surface damage

Safety

Cyclosporine ophthalmic emulsion is contraindicated in those with hypersensitivity to the product.[1,6]

Lifitegrast ophthalmic emulsion has no contraindications.[4]

Neither agents have black box warnings.[1,4,6]

For additional clinical information see the Prime Therapeutics Formulary Chapters 14.1B.

REFERENCES

1. Restasis prescribing information. Allergan, Inc. July 2017.
2. Dry eye syndrome PPP. American Academy of Ophthalmology. September 2013.
3. Ocular Management in Sjögren's Patients. Sjögren's Syndrome Foundation's Clinical Practice Guidelines. Available at https://www.sjogrens.org/home/research-programs/clinical-practice-guidelines. Accessed 2/26/18
4. Xiidra prescribing information. Shire US, Inc. December 2017
5. Summary benchmarks for preferred practice pattern guidelines. American Academy of Ophthalmology. October 2016.
6. Restasis Multidose prescribing information. Allergan, Inc. October 2016.

Document History

Original Prime Standard criteria, approved by P&T UM Committee 04/2015
Client Specific Original Review Prime Standard criteria, approved by BCBS M Pharmacy Clinical Team (PCT) 11/2015
Original Implementation 04/2016
Annual Review Prime Standard criteria, with changes, approved by P&T UM Committee 07/2016
Client Specific Annual Review Prime Standard criteria, with changes, approved by BCBSM PCT 08/2016
Client Specific Annual Review Prime Standard criteria, with changes (updated requirements on Annual Review), approved by BCBS M PCT 10/2016
Administrative Action (NDC update per Medispan for Restasis Multidose bottle) 01/2017
Administrative Action (update textbox) 05/2017
Annual Review Prime Standard criteria, with changes, approved by P&T UM Committee 07/2017
Client Specific Annual Review Prime Standard criteria, with changes, approved by BCBSM PCT 08/2017
Annual Review Prime Standard criteria with changes, approved by P&T UM Committee 06/2018
Client Specific Annual Review Prime Standard criteria, with changes, approved by BCBS M PCT 06/2018

Ophthalmic Immunomodulators Prior Authorization with Quantity Limit

OBJECTIVE
The intent of the Ophthalmic Immunomodulators prior authorization (PA) program is to ensure appropriate selection of patients for treatment according to product labeling and/or clinical studies and/or guidelines. The PA defines appropriate use for Restasis as treatment for patients who have tear production presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca (e.g. Sjögren's Syndrome). The program will not approve for Restasis if the patient is also using a topical ophthalmic anti-inflammatory drug or punctal plug. The program defines appropriate use for Xiidra as treatment for patients with a diagnosis of dry eye disease (dry eye syndrome, keratoconjunctivitis sicca). The program requires patients to have previously tried or are currently using aqueous enhancements. The program will also approve members who have another FDA labeled indication for the requested agent. The program will not approve those with contraindication(s) to the requested agent. The program will not approve for concurrent use of Restasis and Xiidra. Doses above the set limit will be approved if the requested quantity is below the FDA limit or when the quantity is above the FDA limit and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis. Requests will be reviewed when patient-specific documentation has been provided.

TARGET AGENTS
Restasis® (cyclosporine ophthalmic emulsion)
Xiidra™ (lifitegrast ophthalmic solution)

Brand (generic)	GPI/NDC	Multisource Code	Quantity Limit
Restasis (cyclosporine ophthalmic emulsion) multidose bottle	86720020001620 (00023-5301-05)	NA	1 bottle (5.5 mL) / 30 days
Restasis (cyclosporine ophthalmic emulsion) vial	86720020001620	M, N, O, or Y	2 vials / day
Xiidra (lifitegrast ophthalmic solution)	86734050002020	M, N, O, or Y	2 containers / day

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Restasis (cyclosporine ophthalmic emulsion) will be approved when ALL of the following are met:
1. ONE of the following:
    a. ALL of the following:
        i. The patient has a diagnosis of tear production presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca (e.g. Sjögren's Syndrome)
        AND
        ii. ONE of the following:
            1. The patient is not currently using a topical ophthalmic anti-inflammatory drug or punctal plug
            OR
            2. The patient's current use of topical ophthalmic anti-inflammatory drug or punctal plug will be discontinued before starting the requested agent
        AND

iii. ONE of the following:
1. The patient has previously tried or is currently using aqueous enhancements (e.g. artificial tears, gels, ointments [target agents not included])
OR
2. The patient has a documented intolerance, FDA labeled contraindication(s), or hypersensitivity to aqueous enhancements (e.g. artificial tears, gels, ointments [target agents not included])

AND

iv. ONE of the following:
1. The patient is not currently using Xiidra (lifitegrast ophthalmic solution)
OR
2. The patient's current use of Xiidra (lifitegrast ophthalmic solution) will be discontinued before starting the requested agent

OR

b. Other FDA approved indication

AND

2. The patient does not have any FDA labeled contraindication(s) to the requested agent

AND

3. ONE of the following:
a. The requested quantity (dose) is NOT greater than the program quantity limit
OR
b. ALL of the following:
i. The requested quantity (dose) is greater than the program quantity limit
AND
ii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of Approval: 12 months

Xiidra (lifitegrast ophthalmic solution) will be approved when ALL of the following are met:

1. ONE of the following:
a. ALL of the following:
i. The patient has a diagnosis of dry eye disease (i.e. dry eye syndrome, keratoconjunctivitis sicca)
AND
ii. ONE of the following:
1. The patient has previously tried or is currently using aqueous enhancements (e.g. artificial tears, gels, ointments [target agents not included])
OR
2. The patient has a documented intolerance, FDA labeled contraindication(s), or hypersensitivity to aqueous enhancements (e.g. artificial tears, gels, ointments [target agents not included])

AND

iii. ONE of the following:
1. The patient is not currently using Restasis (cyclosporine ophthalmic emulsion)
OR

2. The patient's current use of Restasis (cyclosporine ophthalmic emulsion) will be discontinued before starting the requested agent

OR

b. Other FDA approved indication

AND

2. The patient does not have any FDA labeled contraindication(s) to the requested agent

AND

3. ONE of the following:
   a. The requested quantity (dose) is NOT greater than the program quantity limit

      OR

   b. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit

         AND

      ii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of Approval: 12 months

Ophthalmic Immunomodulators Prior Authorization with Quantity Limit

ELECTRONIC EDIT
The overall process for a prior authorization will not allow the targeted drugs to adjudicate through the claims system. When a patient requests a targeted drug the system will reject the claim with the message indicating that prior authorization is necessary.

PRIOR AUTHORIZATION CRITERIA QUESTION SET
Restasis (cyclosporine ophthalmic emulsion) Evaluation

1. What is the patient's diagnosis?
    a. A diagnosis from Table 1 below:

    Table 1

Diagnoses:
Tear production presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca (e.g. Sjögren's Syndrome)

    b. Another FDA approved diagnosis not listed in Table 1
    c. Other

    If a, continue to 2.
    If b, continue to 8.
    If c, deny.

2. Is the patient currently using a topical ophthalmic anti-inflammatory drug or punctal plug?
    If yes, continue to 3.
    If no, continue 4.

3. Will the current topical ophthalmic anti-inflammatory drug or punctal plug be discontinued before starting the requested agent?
    If yes, continue to 4
    If no, deny.

4. Has the patient previously tried or is the patient currently using aqueous enhancements (e.g. artificial tears, gels, ointments [target agents not included])?
    If yes, continue to 6.
    If no, continue to 5.

5. Does the patient have a documented intolerance, FDA labeled contraindication(s), or hypersensitivity to aqueous enhancements (e.g. artificial tears, gels, ointments [target agents not included])?
    If yes, pharmacist must review and upon approval continue to 6.
    If no, deny.

6. Is the patient currently using Xiidra (lifitegrast ophthalmic solution)?
    If yes, continue to 7.
    If no, continue to 8.

7. Will the current Xiidra (lifitegrast ophthalmic solution) be discontinued before starting the requested agent?
    If yes, continue to 8.
    If no, deny.

8. Does the patient have any FDA labeled contraindication(s) to the requested agent (please see table)?

If yes, deny.
If no, continue to 9.

9. Is the quantity requested greater than the set limit?
   If yes, continue to 10.
   If no, approve for 12 months.

10. Has the prescriber submitted documentation in support of therapy with a higher dose for the intended diagnosis?
    If yes, pharmacist must review and approve quantity requested for 12 months.
    If no, deny for higher quantity. Approve the PA for the set limit for 12 months.

Xiidra (lifitegrast ophthalmic solution) Evaluation

1. What is the patient's diagnosis?
   a. A diagnosis from Table 2 below:

   Table 2

Diagnoses:
dry eye disease (i.e. dry eye syndrome, keratoconjunctivitis sicca)

   b. Another FDA approved diagnosis not listed in Table 2
   c. Other

   If a, continue to 2.
   If b, continue to 6.
   If c, deny.

2. Has the patient previously tried or is the patient currently using aqueous enhancements (e.g. artificial tears, gels, ointments [target agents not included])?
   If yes, continue to 4.
   If no, continue to 3.

3. Does the patient have a documented intolerance, FDA labeled contraindication(s), or hypersensitivity to aqueous enhancements (e.g. artificial tears, gels, ointments [target agents not included])?
   If yes, pharmacist must review and upon approval continue to 4.
   If no, deny.

4. Is the patient currently using Restasis (cyclosporine ophthalmic emulsion)?
   If yes, continue to 5.
   If no, continue to 6.

5. Will the current Restasis (cyclosporine ophthalmic emulsion) be discontinued before starting the requested agent?
   If yes, continue to 6.
   If no, deny.

6. Does the patient have any FDA labeled contraindication(s) to the requested agent (please see table)?
   If yes, deny.
   If no, continue to 7.

7. Is the quantity requested greater than the set limit?
   If yes, continue to 8.
   If no, approve for 12 months.

8. Has the prescriber submitted documentation in support of therapy with a higher dose for the intended diagnosis?
   If yes, pharmacist must review and if approved, approve quantity requested for 12 months.
   If no, deny for higher quantity. Approve the PA for the set limit for 12 months.

FDA Labeled Contraindication(s)

Agent	Contraindication(s)
Restasis (cyclosporine ophthalmic emulsion)	Known or suspected hypersensitivity to any of the ingredients in the formulation.
Xiidra (lifitegrast ophthalmic solution)	None