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

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

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

**FDA APPROVED INDICATIONS AND DOSAGE**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
<th>Dosage and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cequa™</strong> (cyclosporine ophthalmic solution)</td>
<td>Increase tear production in patients with keratoconjunctivitis sicca (dry eye)</td>
<td>One drop twice daily (approximately 12 hours apart) into each eye</td>
</tr>
<tr>
<td><strong>Restasis®</strong> (cyclosporine ophthalmic emulsion)</td>
<td>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.</td>
<td>Instill one drop of ophthalmic emulsion twice a day in each eye approximately 12 hours apart</td>
</tr>
<tr>
<td><strong>Xiidra™</strong> (lifitegrast ophthalmic solution)</td>
<td>Treatment of the signs and symptoms of dry eye disease.</td>
<td>One drop twice daily in each eye (approximately 12 hours apart)</td>
</tr>
</tbody>
</table>

**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:\textsuperscript{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 meibomianitis
- Correction of eyelid abnormality

For treatment of moderate dry eye the following are recommended in addition to mild dry eye treatment options:\textsuperscript{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:\textsuperscript{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.\textsuperscript{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.\textsuperscript{2}

The Sjogren’s Syndrome Foundation’s Clinical Practice Guidelines on Ocular Management in Sjögren Patients states the following.\textsuperscript{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 and cyclosporine ophthalmic solution have no contraindications.⁴,⁷

None of the agents have black box warnings.¹,⁴,⁶,⁷

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

**REFERENCES**

4. Xiidra prescribing information. Shire US, Inc. December 2017
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 Cequa and 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 Cequa, 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
- Cequa™ (cyclosporine ophthalmic solution)
- Restasis® (cyclosporine ophthalmic emulsion)
- Xiidra™ (lifitegrast ophthalmic solution)

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI/NDC</th>
<th>Multisource Code</th>
<th>Quantity Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cequa (cyclosporine ophthalmic solution)</td>
<td>86720020002040</td>
<td>M, N, O, or Y</td>
<td>2 vials / day</td>
</tr>
<tr>
<td>Restasis (cyclosporine ophthalmic emulsion) multidose bottle</td>
<td>86720020001620 (00023-5301-05)</td>
<td>NA</td>
<td>1 bottle (5.5 mL) / 30 days</td>
</tr>
<tr>
<td>Restasis (cyclosporine ophthalmic emulsion) vial</td>
<td>86720020001620</td>
<td>M, N, O, or Y</td>
<td>2 vials / day</td>
</tr>
<tr>
<td>Xiidra (lifitegrast ophthalmic solution)</td>
<td>86734050002020</td>
<td>M, N, O, or Y</td>
<td>2 containers / day</td>
</tr>
</tbody>
</table>

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
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 Cequa (cyclosporine ophthalmic solution) or Xiidra (lifitegrast ophthalmic solution)

OR

2. The patient’s current use of Cequa (cyclosporine ophthalmic solution or 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

Cequa (cyclosporine ophthalmic solution), 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])
iii. ONE of the following:
   1. The patient is not currently using Restasis (cyclosporine ophthalmic emulsion), or Cequa (cyclosporine ophthalmic solution) if requesting Xiidra (lifitegrast ophthalmic solution), or Xiidra (lifitegrast ophthalmic solution) if requesting Cequa (cyclosporine ophthalmic solution)
      OR
   2. The patient’s current use of Restasis (cyclosporine ophthalmic emulsion), or Cequa (cyclosporine ophthalmic solution) if requesting Xiidra (lifitegrast ophthalmic solution), or Xiidra (lifitegrast ophthalmic solution) if requesting Cequa (cyclosporine 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
Step Therapy Supplement

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

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT

OBJECTIVE
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL
The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
   a. A statement by the prescriber that the patient is currently taking the requested agent
   AND
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
   AND
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

OR

2. The patient’s medication history include the required prerequisite/preferred agent(s) as indicated by:
   a. Evidence of a paid claim(s) within the past 999 days
   OR
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event

OR

3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria