Ophthalmic Immunomodulators Prior Authorization with Quantity Limit Program Summary

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

This is a FlexRx Standard and GenRx Standard program.

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

POLICY REVIEW CYCLE

Effective Date	Date of Origin
04-01-2024	04-01-2016

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Cequa® (cyclosporine) Ophthalmic solution	Increase tear production in patients with keratoconjunctivitis sicca (dry eye)		1
Restasis® (cyclosporine) * Ophthalmic e mulsion	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.	*generic available	2
Verkazia® (cyclosporine) Ophthalmic emulsion	Treatment of vernal keratoconjunctivitis (VKC) in children and adults		10
Vevye™ (cyclosporine) Ophthalmic solution	Treatment of the signs and symptoms of dry eye disease		13
Xiidra® (lifitegrast) Ophthalmic solution	Treatment of the signs and symptoms of dry eye disease		3

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Dry Eye Disease	Dry eye disease (also known as dry eye syndrome) is a multifactorial disease of the ocular surface with loss of homeostasis of the tear film. It is accompanied by ocular symptoms where tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.(6) The tear film secreting glands and ocular surface function as an integrated system. Disease or dysfunction of this system results in unstable and poorly maintained tear film that causes symptoms of ocular irritation and possible damage to the ocular surface. Dry eye disease may be exacerbated by systemic medications (e.g., diuretics, antihistamines, anticholinergics, systemic retinoids, antidepressants) and rosacea.(4) Dry eye disease is often associated with Sjogren syndrome, an autoimmune multisystem disorder that most often affects the tear and salivary glands. Tear deficiency may occur in other systemic diseases, such as lymphoma, sarcoidosis, hemochromatosis, and amyloidosis. Dry eye disease may also develop due to systemic viral infections, such as retroviruses, Epstein-Barr virus, and HIV.(4) The American Academy of Ophthalmology and the Tear Film and Ocular Surface Society (TFOS) categorized dry eye into three severity levels based on both symptoms and signs. Due to the nature of the disease, this classification is imprecise because the characteristics overlap at each level of severity.(4,6,7) • 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 visual symptoms that may become constant as well as potentially disabling The American Academy of Ophthalmology recommend treating mild dry eye with the following:(4,8) • 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:(4,8) • 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:(4,8) • Systemic cholinergic agonists • Mucolytic agents • Autologous serum tears • Therapeutic contact lenses • Surgical 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.(4) 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.(4) Pre-treatment with topical ophthalmic corticosteroids either before or during initiation with a non-glucocorticoid anti-inflammatory agent may provide more rapid improvement in symptoms of dry eye disease and decrease the incidence of severe stinging associated with a topical immunomodulator agent compared to a topical immunomodulator alone.(8) The AAO also notes that topical corticosteroid use for dry eye disease is controversial, but use for induction therapy prior to initiating non-glucocorticoid anti-inflammatory agents as maintenance. Once the patient is in a successful maintenance phase, steroids are used for acute flare-ups triggered by travel, allergies, respiratory infections, or exposures to environmental irritants with maintenance therapy.(9) The Sjogren's Syndrome Foundation's Clinical Practice Guidelines on Ocular Management in Sjögren's Patients states the following.(5) • Management depends upon the nature of the dry and the severity of symptoms. • 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.
Vernal Keratoconjunctivitis	Vernal keratoconjunctivitis (VKC) is an atopic condition of the external ocular surface. VKC is typically seen in hot, dry climates. Symptoms typically present in early to mid-childhood and typically resolves after puberty. Symptoms may include eye itching, photophobia, tearing, ocular discharge, irritation, redness, and blepharospasm. VKC can be divided into three subcategories based on the presentation of disease, conjunctival, limbal, and mixed presentation. VKC is both an IgE and non-IgE mediated ocular allergic condition.(11,12)

	Treatment follows a step wise approach based on disease severity (11,12) • Topical mast cell stabilizers and antihistamines for patients with micropapillae and no corneal changes • Topical corticosteroids for patients with macropapillae, mucus accumulation, and corneal vascularization • Immunomodulating agents for patients with macropapillae, macroerosion, shield ulcer, and persistent severe inflammation Topical antihistamines and topical mast cell stabilizers in combination with pulse corticosteroids during an exacerbation is common practice for maintenance of VKC.(11,12) The American Academy of Ophthalmology Preferred Practice Pattern indicate that topical mast cell stabilizers in combination with topical or oral antihistamines can be used for maintenance. The AAO also recommends topical ophthalmic corticosteroids for acute exacerbations to control severe symptoms and signs. Topical cyclosporine may allow for reduced used of topical steroids.(12)
Safety	Restasis (cyclosporine) is contraindicated in patients with hypersensitivity to any of the ingredients in the formulation.(2) Xiidra (lifitegrast) is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients in the formulation.(3) Cequa (cyclosporine), Verkazia (cyclosporine), and Vevye (cyclosporine) have no FDA labeled contraindications for use.(1,10,13)

REFERENCES

Number	Reference
1	Cequa prescribing information. Sun Pharma Global. December 2022.
2	Restasis prescribing information. Allergan, Inc. July 2017.
3	Xiidra prescribing information. Shire US, Inc. June 2020.
4	Dry eye syndrome Preferred Practice Pattern. American Academy of Ophthalmology. October 2018. https://doi.org/10.1016/j.ophtha.2018.10.023
5	Ocular Management in Sjögren's Patients. Sjögren's Syndrome Foundation's Clinical Practice Guidelines. https://sjogrens.org/sites/default/files/inline-files/SF_CPG-Ocular_2022_0.pdf
6	Craig, J. P., Nichols, K. K., Akpek, E. K., Caffery, B., Dua, H. S., Joo, C.-K., Liu, Z., Nelson, J. D., Nichols, J. J., Tsubota, K., & Stapleton, F. (2017). TFOS DEWS II definition and classification report. The Ocular Surface, 15(3), 276–283. https://doi.org/10.1016/j.jtos.2017.05.008
7	Wolffsohn, J. S., Arita, R., Chalmers, R., Djalilian, A., Dogru, M., Dumbleton, K., Gupta, P. K., Karpecki, P., Lazreg, S., Pult, H., Sullivan, B. D., Tomlinson, A., Tong, L., Villani, E., Yoon, K. C., Jones, L., & Craig, J. P. (2017). TFOS DEWS II Diagnostic Methodology Report. The Ocular Surface, 15(3), 539–574. https://doi.org/10.1016/j.jtos.2017.05.001
8	Jones, L., Downie, L. E., Korb, D., Benitez-del-Castillo, J. M., Dana, R., Deng, S. X., Dong, P. N., Geerling, G., Hida, R. Y., Liu, Y., Seo, K. Y., Tauber, J., Wakamatsu, T. H., Xu, J., Wolffsohn, J. S., & Craig, J. P. (2017). TFOS DEWS II management and therapy report. The Ocular Surface, 15(3), 575–628. https://doi.org/10.1016/j.jtos.2017.05.006
9	Weiner, G. Savvy steroid use. American Academy of Ophthalmology. (2016, May 5). https://www.aao.org/eyenet/article/savvy-steroid-use
10	Verkazia prescribing information. Santen Inc. June 2022.

Number	Reference
11	Kraus, C. L. (2018, January 17). Vernal keratoconjunctivitis. American Academy of Ophthalmology. https://www.aao.org/education/disease-review/vernal-keratoconjunctivitis-5
12	Varu, D. M., Rhee, M. K., Akpek, E. K., Amescua, G., Farid, M., Garcia-Ferrer, F. J., Lin, A., Musch, D. C., Mah, F. S., & Dunn, S. P. (2018). Conjunctivitis preferred practice pattern®. Ophthalmology, 126(1), 94–169. https://doi.org/https://doi.org/10.1016/j.ophtha.2018.10.020
13	Vevye prescribing information. Novaliq GmbH. May 2023.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Restasis ; Restasis multidose	Cyclosporine (Ophth) Emulsion 0.05%	0.05 %	M ; N ; O ; Y	O ; Y		
Cyclosporine in klarity ; Verkazia	Cyclosporine (Ophth) Emulsion 0.1%	0.1 %	M ; N ; O ; Y	N		
Cequa ; Vevye	cyclosporine (ophth) soln	0.09 % ; 0.1 %	M ; N ; O ; Y	N		
Xiidra	lifitegrast ophth soln	5 %	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Cequa	Cyclosporine (Ophth) Soln 0.09% (PF)	0.09 %	60	Vials	30	DAYS			
Cyclosporine in klarity ; Verkazia	Cyclosporine (Ophth) Emulsion 0.1%	0.1 %	120	Vials	30	DAYS			
Restasis	cyclosporine (ophth) emulsion	0.05 %	60	Vials	30	DAYS			00023916330 ; 00023916360 ; 00378876058 ; 00378876091 ; 10702080803 ; 10702080806 ; 50090124200 ; 50090447600 ; 60505620201 ; 60505620202 ; 68180021430 ; 68180021460
Restasis ; Restasis multidose	cyclosporine (ophth) emulsion	0.05 %	1	Bottle	30	DAYS			00023530105 ; 50090447600

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Vevye	cyclosporine (ophth) soln	0.1 %	1	Bottle	30	DAYS			
Xiidra	Lifitegrast Ophth Soln 5%	5 %	60	Vials	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Cequa ; Vevye	cyclosporine (ophth) soln	0.09 % ; 0.1 %	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Cyclosporine in klarity ; Verkazia	Cyclosporine (Ophth) Emulsion 0.1%	0.1 %	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Restasis ; Restasis multidose	Cyclosporine (Ophth) Emulsion 0.05%	0.05 %	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Xiidra	lifitegrast ophth soln	5 %	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Cequa	Cyclosporine (Ophth) Soln 0.09% (PF)	0.09 %	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Cyclosporine in klarity ; Verkazia	Cyclosporine (Ophth) Emulsion 0.1%	0.1 %	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Restasis	cyclosporine (ophth) emulsion	0.05 %	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Restasis ; Restasis multidose	cyclosporine (ophth) emulsion	0.05 %	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Vevye	cyclosporine (ophth) soln	0.1 %	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
			Insurance Marketplace/BasicRx ; KeyRx
Xiidra	Lifitegrast Ophth Soln 5%	5 %	FlexRx Closed ; FlexRx Open ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Restasis (cyclosporine ophthalmic emulsion)** will be approved when ALL of the following are met: 1. ONE of the following: A. ALL of the following: 1. The patient has a diagnosis of dry eye disease (i.e., dry eye syndrome, keratoconjunctivitis sicca [e.g., Sjögren's Syndrome]) **AND** 2. The patient will NOT be using the requested agent in combination with punctal plug(s) **AND** 3. ONE of the following: A. The patient has previously tried or is currently using aqueous enhancements (e.g., artificial tears, gels, ointments [target agents not included]) **OR** B. The patient has an intolerance or hypersensitivity to aqueous enhancements (e.g., artificial tears, gels, ointments [target agents not included]) **OR** C. The patient has an FDA labeled contraindication to ALL aqueous enhancements **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on the requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL aqueous enhancements 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 **OR** B. The patient has another FDA approved indication for the requested agent **AND** 2. The patient will NOT be using the requested agent in combination with another ophthalmic immunomodulator agent (e.g., Restasis, Cequa, Xiidra, Verkazia, Vevye) or Tyrvaya **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 6 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

Module	Clinical Criteria for Approval
	Initial Evaluation **Cequa (cyclosporine), Xiidra (lifitegrast), Vevye (cyclosporine)** will be approved when ALL of the following are met: 1. ONE of the following: A. BOTH of the following: 1. The patient has a diagnosis of dry eye disease (i.e., dry eye syndrome, keratoconjunctivitis sicca [e.g., Sjögren's Syndrome]) **AND** 2. ONE of the following: A. The patient has previously tried or is currently using aqueous enhancements (e.g., artificial tears, gels, ointments [target agents not included]) **OR** B. The patient has an intolerance or hypersensitivity to aqueous enhancements (e.g., artificial tears, gels, ointments [target agents not included]) **OR** C. The patient has an FDA labeled contraindication to ALL aqueous enhancements **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on the requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL aqueous enhancements 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 **OR** B. The patient has another FDA approved indication for the requested agent **AND** 2. The patient will NOT be using the requested agent in combination with another ophthalmic immunomodulator agent (e.g., Restasis, Cequa, Xiidra, Verkazia, Vevye) or Tyrvaya **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** Cequa (cyclosporine), Xiidra (lifitegrast) Vevye (cyclosporine) - 3 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Initial Evaluation** **Verkazia (cyclosporine)** will be approved when ALL of the following are met: 1. ONE of the following: A. The patient has a diagnosis of vernal keratoconjunctivitis (VKC) AND BOTH of the following: 1. ONE of the following: A. The patient has tried and had an inadequate response to combination of a topical ophthalmic mast cell stabilizer AND an antihistamine used in the treatment of VKC **OR** B. The patient has an intolerance or hypersensitivity to combination of a topical ophthalmic mast cell stabilizer AND an antihistamine used in the treatment of VKC **OR** C. The patient has an FDA labeled contraindication to ALL topical ophthalmic mast cell stabilizers AND antihistamines **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following:

Module	Clinical Criteria for Approval
	1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on the requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL topical ophthalmic mast cell stabilizers AND antihistamines 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 **AND** 2. ONE of the following: A. The patient has tried and had an inadequate response to a topical ophthalmic corticosteroid used in the treatment of VKC **OR** B. The patient has an intolerance or hypersensitivity to topical ophthalmic corticosteroid therapy **OR** C. The patient has an FDA labeled contraindication to ALL topical ophthalmic corticosteroids **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on the requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL topical ophthalmic corticosteroids 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 **AND** B. The patient has another FDA approved indication for the requested agent **AND** 2. The patient will NOT be using the requested agent in combination with another ophthalmic immunomodulator agent (e.g., Restasis, Cequa, Xiidra, Verkazia, Vevye) or Tyrvaya **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 4 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The patient will NOT be using the requested agent in combination with another ophthalmic immunomodulator agent (e.g., Restasis, Cequa, Xiidra, Verkazia, Vevye) or Tyrvaya **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent

Module	Clinical Criteria for Approval
	Length of Approval: 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. BOTH of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **Length of Approval**: Initial - Cequa, Xiidra, Vevye - 3 months, Verkazia - 4 months, Restasis/cyclosporine - 6 months Renewal - 12 months