Drug Coverage Policy

Effective Date……09/15/2025
Coverage Policy Number……IP0026
Policy Title….. Cyclosporine Ophthalmic Products

Ophthalmology – Dry Eye Disease Cyclosporine Ophthalmic Products

- Cequa™ (cyclosporine 0.09% ophthalmic solution – Sun Pharmaceuticals)
- Restasis® (cyclosporine 0.05% ophthalmic emulsion - Allergan, generic)
- Restasis Multidose™ (cyclosporine 0.05% ophthalmic emulsion - Allergan)
- Vevye™ (cyclosporine 0.1% ophthalmic solution – Harrow)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview
Ophthalmic cyclosporine products are generally indicated for the treatment of signs and symptoms of **dry eye disease**.[1-4] Specifically, ophthalmic cyclosporine emulsion products are indicated to increase tear production in patients whose tear production is presumed to be suppressed due to **ocular inflammation associated with keratoconjunctivitis sicca**.[1,2] Cequa is indicated to increase tear production in patients with **keratoconjunctivitis sicca** (dry eye).[3] Vevye is indicated for the treatment of the signs and symptoms of **dry eye disease**.[4]

Dry eye disease refers to a group of disorders of the tear film that are due to reduced tear production or tear instability and are associated with ocular discomfort and inflammatory disease of the ocular surface.[5] Dry eye disease is also known as dry eye syndrome and keratoconjunctivitis sicca.

The safety and efficacy of Restasis have not been established in pediatric patients < 16 years of age.[1,2] Both Cequa and Vevye are approved for use in patients ≥ 18 years of age per product labeling.[3,4] All of these products have the same chemical moiety (cyclosporine).[1-4]

Guidelines
The American Academy of Ophthalmology (AAO) Dry Eye Syndrome Preferred Practice Pattern® [2024] notes dry eye syndrome is also known as dry eye disease or keratoconjunctivitis sicca.[2] Dry eye is generally classified according to both symptoms and signs (i.e., mild, moderate, or severe); however, there is an emphasis on symptoms over signs. Management of dry eye is listed as a four-step staged approach, but specific therapies may be chosen from any step, regardless of the level of disease severity, depending on provider experience and patient preference. Ophthalmic cyclosporine products, as well as other FDA-approved therapies for dry eye disease (Miebo™ [perfluorohexyloctane ophthalmic solution], Tyrvaya® [varenicline nasal spray], and Xiidra® [lifitegrast ophthalmic solution]), are noted as Step 2 options in the Preferred Practice Pattern. The AAO notes use of any of these FDA-approved products may lead to improvement of patient symptoms and/or signs but none has been proven more effective than the other in head-to-head trials; there are no direct comparisons in a prospective clinical trial in the literature. The AAO also notes that dry eye disease may develop as a result of systemic inflammatory diseases (e.g., Sjögren syndrome, autoimmune thyroid disease, or rheumatoid arthritis) and ocular surface disease (e.g., herpes simplex virus keratitis).

The AAO Blepharitis Preferred Practice Pattern® (2024) note that blepharitis can be classified according to anatomic location; anterior blepharitis affects the eyelid skin, base of the eyelashes and the eyelash follicles, whereas posterior blepharitis affects the meibomian glands. Blepharitis frequently leads to ocular surface inflammation, including conjunctivitis, functional tear deficiency, and keratitis and may exacerbate symptoms of coexisting ocular surface disease (including allergy and aqueous tear deficiency).[6] Treatment of blepharitis includes use of warm compresses, eyelid cleansing/eyelid massages, topical and/or systemic antibiotics, and ophthalmic anti-inflammatory agents (e.g., corticosteroids, cyclosporine).

The AAO Conjunctivitis Preferred Practice Pattern® guidelines for conjunctivitis (2024) note that dry eye and blepharitis are the most frequent causes of conjunctival inflammation.[7] Ophthalmic cyclosporine can be used to treat dry eye syndrome associated with GVHD and different types of conjunctivitis.

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for benefit coverage of ophthalmic cyclosporine products. All approvals are provided for the duration noted below.

Ophthalmic cyclosporine products are considered medically necessary when ONE of the following are met (1, 2, or 3):

FDA-Approved Indication

1. **Dry Eye Disease.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A. Patient is ≥ 16 years of age; AND
   B. Preferred product criteria is met for the product(s) as listed in the below table(s)
   Note: Examples of dry eye disease include dry eye syndrome and keratoconjunctivitis sicca.

Other Uses with Supportive Evidence

2. **Dry Eye Conditions due to Systemic Inflammatory Diseases.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A. Patient is ≥ 16 years of age; AND
   B. Preferred product criteria is met for the product(s) as listed in the below table(s)
   Note: Examples of systemic inflammatory diseases that could result in dry eye conditions include Sjögren syndrome, autoimmune thyroid disease, rheumatoid arthritis.

3. **Dry Eye Conditions due to Ocular Surface Diseases.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A. Patient is ≥ 16 years of age; AND
   B. Preferred product criteria is met for the product(s) as listed in the below table(s)
   Note: Examples of ocular surface diseases that could result in dry eye conditions include blepharitis, conjunctivitis, herpes simplex keratitis, ocular graft-versus-host disease.

Employer Plans:

Product	Criteria
Restasis Multidose (cyclosporine topical emulsion) 0.05%	**ONE** of the following (1 or 2): **1.** Patient has tried, and according to the prescriber, has experienced inadequate efficacy OR significant intolerance with cyclosporine ophthalmic 0.05% emulsion **2.** Patient is unable to use generic cyclosporine 0.05% ophthalmic emulsion single use vials, patient meets ONE of the following (A or B) A. Patient has tried, and according to the prescriber, has experienced inadequate efficacy OR significant intolerance with BOTH of the following products (i and ii): i. Cequa ii. Xiidra B. If the patient is currently receiving therapy with Restasis Multidose, the patient has tried, and according to the prescriber, has experienced inadequate efficacy OR significant intolerance with Cequa
Vevye	**ONE** of the following (1 or 2):

Product	Criteria
(cyclosporine ophthalmic drops) 0.1%	**1.** Patient has tried, and according to the prescriber, has experienced inadequate efficacy OR significant intolerance with TWO of the following products (A, B, C): A. generic cyclosporin topical emulsion B. Cequa (cyclosporine 0.09% ophthalmic solution) C. Xiidra (lifitegrast ophthalmic solution) **2.** Patient is currently receiving therapy with Vevye, AND has tried, and according to the prescriber, has experienced inadequate efficacy OR significant intolerance with ONE of the following products (A or B): A. generic cyclosporin topical emulsion B. Cequa (cyclosporine 0.09% ophthalmic solution)

Individual and Family Plans:

Product	Criteria
Cequa (cyclosporine 0.09% ophthalmic solution)	Patient has tried, and according to the prescriber, has experienced inadequate efficacy OR significant intolerance with cyclosporine ophthalmic 0.05% emulsion
Restasis (cyclosporine topical emulsion) 0.05%	Patient has tried bioequivalent generic product, **cyclosporine topical emulsion** AND cannot take due to a formulation difference in the inactive ingredient(s) [for example, difference in dyes, fillers, preservatives] between the Brand and the bioequivalent generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction
Restasis Multidose (cyclosporine topical emulsion) 0.05%	**ONE** of the following (1 or 2): **1.** Patient has tried, and according to the prescriber, has experienced inadequate efficacy OR significant intolerance with cyclosporine ophthalmic 0.05% emulsion **2.** Patient is unable to use generic cyclosporine 0.05% ophthalmic emulsion single use vials
Vevye (cyclosporine ophthalmic drops) 0.1%)	Patient has tried, and according to the prescriber, has experienced inadequate efficacy OR significant intolerance with cyclosporine ophthalmic 0.05% emulsion

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Ophthalmic cyclosporine products for any other use are considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concomitant Use with Another Ophthalmic Cyclosporine Product, Tryptyr (acolmetron ophthalmic solution), Tyrvaya (varenicline nasal solution), or Xiidra (lifitegrast ophthalmic solution).** There are no data to support the concomitant use of two (or three) ophthalmic cyclosporine products or the concomitant use of an ophthalmic cyclosporine product with Tryptyr, Tyrvaya, or Xiidra.
   Note: Ophthalmic cyclosporine products are Cequa, Restasis, and Vevye.

References

1. Restasis® ophthalmic emulsion 0.05% [prescribing information]. North Chicago, IL: AbbVie; September 2024.
2. Restasis Multidose™ ophthalmic emulsion 0.05% [prescribing information]. North Chicago, IL: AbbVie; September 2024.
3. Cequa™ ophthalmic solution [prescribing information]. Cranbury, NJ: Sun Pharmaceutical; July 2022.
4. Vevye™ ophthalmic solution, 0.1%. Nashville, TN: Harrow; May 2024.
5. Amescua G, Ahmad S, Cheung AY, et al. American Academy of Ophthalmology Preferred Practice Pattern Cornea and External Disease Panel. Dry Eye Syndrome Preferred Practice Pattern®. *Ophthalmology*. 2024;131(4);P1-P49.
6. Lin A, Ahmad S, Amescua Get al. American Academy of Ophthalmology Preferred Practice Pattern Cornea and External Disease Panel. Blepharitis Preferred Practice Pattern®. *Ophthalmology*. 2024;131(4):P50-P86...
7. Cheung AY, Choi DS, Ahmad S, et al. American Academy of Ophthalmology Preferred Practice Pattern Cornea and External Disease Panel. Conjunctivitis Preferred Practice Pattern®. *Ophthalmology*. 2024;131(4):P134-P204.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Added** diagnosis and age requirements. **Updated** the Restasis and Restasis Multidose criteria for Employer plans. **Updated** the Vevye criteria for Employer plans and Individual and Family Plans. **Updated** and **added** the Cequa, Restasis and Restasis Multidose criteria for Individual and Family plans. **Conditions Not Covered:** Miebo was removed from the criterion "Concomitant Use with Another Ophthalmic Cyclosporine Product, Miebo (perfluorohexyloctane ophthalmic solution), Tyrvaya (varenicline nasal spray), or Xiidra (lifitegrast ophthalmic solution)" because Miebo can be used concomitantly with these agents.	08/01/2024

Annual Revision	**Employer Plan Preferred Product Table. Restasis Multidose: Added** preferred product step requirements for when patient is unable to use generic cyclosporine 0.05% ophthalmic emulsion single use vials	08/01/2025
Selected Revision	**Employer Plan Preferred Product Table. Removed** Restasis vial preferred product requirements.	09/01/2025
Selected Revision	**Conditions Not Recommended for Approval:** Tryptyr was added to the list of medications that should not be used concomitantly with the requested cyclosporine product.	09/15/2025

The policy effective date is in force until updated or retired.