VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Ophthalmic for Dry Eye Disease – Cyclosporine Products Prior Authorization Policy
- Cequa™ (cyclosporine topical solution – Sun Pharmaceuticals)
- Restasis and Restasis Multidose™ (cyclosporine topical emulsion – Allergan)

REVIEW DATE: 08/19/2020

OVERVIEW

Restasis (cyclosporine topical emulsion), an immunosuppressive agent, is 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] The safety and efficacy of Restasis have not been established in pediatric patients < 16 years of age.

Cequa is a topical solution of cyclosporine, with the same active ingredient and mechanism as Restasis.[3] Although Cequa is approved for patients ≥ 18 years of age per product labeling, it has the same active chemical moiety as Restasis, which is approved in patients ≥ 16 years of age.[1-3] Cequa has a novel formulation in which the hydrophobic cyclosporine molecules are encased in nanomicelles with a hydrophilic exterior.[4] This facilitates crossing of the corneal barrier and penetration of the aqueous humor to reach ocular tissues.

Other Uses with Supportive Evidence

Systemic Inflammatory Diseases

Patients with primary Sjögren syndrome have nonclassifiable systemic disease, whereas patient with secondary Sjögren syndrome have a distinct autoimmune disease such as rheumatoid arthritis, systemic lupus erythematosus, or scleroderma. A 2010 systematic review of randomized controlled trials for the treatment of primary Sjögren syndrome found topical cyclosporine to be effective for moderate or severe dry eye symptoms.[7]

Ocular Surface Diseases

There are some efficacy data to support the off-label use of topical cyclosporine in the treatment of immune-mediated ocular surface diseases such as ocular rosacea and atopic keratoconjunctivitis.[6,8-11] A review article noted that dosing of Restasis at a frequency greater than twice daily (BID) regimen may be beneficial for patients with severe dry eye disease, such as ocular graft versus host disease (GVHD), if they do not initially respond to the BID regimen.[12] Also, it has been suggested that initiation of topical cyclosporine prior to bone marrow transplantation may reduce inflammatory response in the lacrimal gland and could reduce dry eye symptoms post-transplant.

Guidelines

The American Academy of Ophthalmology (AAO) published Preferred Practice Pattern® (2018) for the treatment of dry eye syndrome.[5] The AAO classifies dry eye as mild, moderate, or severe, based on signs and symptoms of the disease. Treatment recommendations of dry eye disease are listed in a four step progression but specific therapies may be chosen from any category regardless of the level of disease severity, depending on provider experience and patient preference. Topical nonglucocorticoid immunomodulatory drugs (such as cyclosporine) are staged as a Step 2 recommendation within the guidelines. The AAO recommends the use of topical cyclosporine as one of the treatment options for Sjögren syndrome. The AAO states that topical cyclosporine may be useful in some patients with posterior blepharitis, in active ocular GVHD, and as adjunctive treatment in atopic/vernal conjunctivitis.[13-14]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Restasis and Cequa. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Restasis and Cequa is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Dry Eye Conditions due to Ocular Inflammation Associated with Keratoconjunctivitis Sicca (e.g., dry eye syndrome or dry eye disease).** Approve for 3 years if the patient is ≥ 16 years of age.

Other Uses with Supportive Evidence

2. **Dry Eye Conditions due to Systemic Inflammatory Diseases (e.g., Sjögren syndrome, rheumatoid arthritis, systemic lupus erythematosus).** Approve for 3 years if the patient is ≥ 16 years of age.

3. **Dry Eye Conditions due to Ocular Surface Diseases (e.g., ocular rosacea, atopic keratoconjunctivitis, acute corneal graft rejection, blepharitis, herpetic stromal keratitis, conjunctival graft versus host disease).** Approve for 3 years if the patient is ≥ 16 years of age.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Restasis and Cequa is not recommended in the following situations:

1. **Concomitant use with Xiidra™ (lifitegrast ophthalmic solution).** There are no data to support the concomitant use of Restasis or Cequa and Xiidra.

2. **Concomitant use of Cyclosporine Products.** There is no evidence to support additive efficacy of combining Restasis and Cequa.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Restasis® ophthalmic emulsion 0.05% [prescribing information]. Irvine, CA: Allergan, Inc.; July 2017.
2. Restasis Multidose™ ophthalmic emulsion 0.05% [prescribing information]. Irvine, CA: Allergan; July 2017.
3. Cequa™ ophthalmic solution [prescribing information]. Cranbury, NJ: Sun Pharmaceutical Industries; August 2018.
4. Data on file. Cequa® Product Dossier. Based on AMCP guidelines for formulary submission. Sun Pharmaceutical Industries, Inc.; August 2018.
5. American Academy of Ophthalmology cornea/external disease panel. Preferred practice pattern® guidelines. Dry eye syndrome. San Francisco, CA: American Academy of Ophthalmology; 2018. Available at: www.aao.org/ppp. Accessed on August 11, 2020.
6. Yagci A, Gurdal C. The role and treatment of inflammation in dry eye disease. *Int Ophthalmol*. 2014;34(6):1291-1301.
7. Ramos-Casals M, Tzioufas AG, Stone JH, et al. Treatment of primary Sjogren syndrome – a systematic review. *JAMA.* 2010;304:452-460.
8. Utine CA, Stern M, Akpek EK. Clinical review: Topical ophthalmic use of cyclosporine A. *Ocul Immunol Inflamm.* 2010;18:352-361.
9. Hessen M, Akpek EK. Ocular graft-versus-host disease. *Curr Opin Allergy Clin Immunol*. 2012;12:540-547.
10. Van Zuuren EJ, Fedorowicz Z, Carter B, et al. Interventions for rosacea (review). The Cochrane Collaboration®. *Cochrane Database Syst Rev.* 2015;4:CD003262.
11. Arman A, Demirseren DD, Takmaz T. Treatment of ocular rosacea: comparative study of topical cyclosporine and oral doxycycline. *Int J Ophthalmol*. 2015;8(3):544-549.
12. Donnenfeld E, Pflugfelder SC. Topical ophthalmic cyclosporine: pharmacology and clinical uses. *Surv Ophthalmol.* 2009;54:321-338.
13. American Academy of Ophthalmology cornea/external disease panel. Preferred practice pattern® guidelines. Blepharitis. San Francisco, CA: American Academy of Ophthalmology; 2018. Available at: www.aao.org/ppp. Accessed on August 11, 2020.
14. American Academy of Ophthalmology cornea/external disease panel. Preferred practice pattern® guidelines. Conjunctivitis. San Francisco, CA: American Academy of Ophthalmology; 2018. Available at: www.aao.org/ppp. Accessed on August 11, 2020.