Clinical Policy: Cyclosporine (Cequa, Restasis, Verkazia, Vevye)

Reference Number: CP.PMN.48
Effective Date: 05.01.12
Last Review Date: 05.23
Line of Business: Commercial*, HIM, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Cyclosporine ophthalmic (Cequa™, Restasis®, Verkazia®, Vevye™) is a topical calcineurin inhibitor immunosuppressant.

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***For Commercial,** if request is through pharmacy benefit, Cequa is non-formulary and should not be approved using these criteria; refer to the formulary exception policy, CP.CPA.190. Restasis does not require prior authorization.*

FDA Approved Indication(s)

Cequa is indicated to increase tear production in patients with keratoconjunctivitis sicca (dry eye).

Restasis is 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.

Verkazia is indicated for the treatment of vernal keratoconjunctivitis (VKC) in children and adults.

Vevye is indicated for the treatment of the signs and symptoms of dry eye disease.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Cequa, Restasis, Verkazia, and Vevye are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Keratoconjunctivitis Sicca (must meet all)**:**

1. Diagnosis of keratoconjunctivitis sicca (dry eye) with suppressed tear production due to ocular inflammation;
2. Request is for Cequa, Restasis, or Vevye;
3. Member meets one of the following (a or b):
   a. For Restasis: Age ≥ 16 years;
   b. For Cequa or Vevye: Age ≥ 18 years;

4. Failure of artificial tears at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of at least one ophthalmic anti-inflammatory agent (*see Appendix B for examples*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Member must use generic ophthalmic cyclosporine emulsion 0.05% (generic Restasis), unless contraindicated or clinically significant adverse effects are experienced;
7. The requested agent is not prescribed in combination with other ophthalmic cyclosporine products (e.g., Verkazia);
8. Request does not exceed either of the following (a or b):
   a. For Cequa or Restasis: 60 vials per 30 days;
   b. For Vevye: 1 bottle per 50 days.

Approval duration:
Commercial – 6 months for Vevye *(Restasis does not require prior authorization; refer to CP.CPA.190 for Cequa)*
HIM – 6 months
Medicaid – Length of Benefit

B. Vernal Keratoconjunctivitis (must meet all)**:**
1. Diagnosis of VKC;
2. Request is for Verkazia;
3. Age ≥ 4 years;
4. Failure of artificial tears at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of a topical mast cell stabilizer and topical antihistamine (as a single dual-acting product or as two products used in combination; *see Appendix B for examples*) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
6. Verkazia is not prescribed in combination with other ophthalmic cyclosporine products (e.g., Cequa, Restasis, Vevye);
7. Request does not exceed 120 vials per affected eye per 30 days.

Approval duration: 6 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Keratoconjunctivitis Sicca (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Request is for Cequa, Restasis, or Vevye;
3. Member is responding positively to therapy;
4. Member must use generic ophthalmic cyclosporine emulsion 0.05% (generic Restasis), unless contraindicated or clinically significant adverse effects are experienced;
5. The requested agent is not prescribed in combination with other ophthalmic cyclosporine products (e.g., Verkazia);
6. If request is for a dose increase, request does not exceed one of the following (a or b):
   a. For Cequa or Restasis: 60 vials per 30 days;
   b. For Vevye: 1 bottle per 50 days.

Approval duration:
Commercial – 6 months for Vevye *(Restasis does not require prior authorization; refer to CP.CPA.190 for Cequa)*
HIM – 12 months
Medicaid – Length of Benefit

B. Vernal Keratoconjunctivitis (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Request is for Verkazia;
3. Member is responding positively to therapy;
4. Verkazia is not prescribed in combination with other ophthalmic cyclosporine products (e.g., Cequa, Restasis, Vevye);
5. If request is for a dose increase, request does not exceed 120 vials per affected eye per 30 days.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
VKC: vernal keratoconjunctivitis

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
artificial tears (e.g., Visine dry eye relief)	1 to 2 drops in affected eye(s) BID or QID	Various
ophthalmic anti-inflammatory agents for keratoconjunctivitis sicca (e.g., loteprednol etabonate) Note: Ophthalmic NSAIDs are not indicated.	1 to 2 drops in each eye BID to QID for up to 2 weeks	Various
topical dual-acting mast cell stabilizer/antihistamine for VKC	1 to 2 drops in affected eye(s) per day	Various

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
(e.g., azelastine, bepotastine, epinastine, ketotifen, olopatadine)		
topical mast cell stabilizer for VKC (e.g., cromolyn, lodoxamide, nedocromil)	2 to 6 drops in affected eye(s) per day	Various
topical antihistamine for VKC (e.g., alcaftadine, emedastine)	1 to 4 drops in affected eye(s) per day	Various

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Cequa, Verkazia, Vevye: none reported
  - Restasis: hypersensitivity to cyclosporine or any of the ingredients in the formulation
- Boxed warning(s): none reported

Appendix D: General Information

- Artificial tears are the standard therapy for all severity of dry eyes.
- Restasis is likely to be given in conjunction with artificial tears.
- Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs.
- Emulsion from one individual, single-use vial is to be used immediately after opening for administration to one or both eyes, and the remaining contents should be discarded immediately after administration.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Cyclosporine ophthalmic solution (Cequa, Restasis)	Moderate to severe keratoconjunctivitis sicca	1 drop BID in each eye approximately 12 hours apart	2 drops/day in each eye; 60 vials/30 days
Cyclosporine ophthalmic solution (Vevye)	Dry eye disease	1 drop BID in each eye approximately 12 hours apart	2 drops/day in each eye; 1 bottle/50 days
Cyclosporine ophthalmic solution (Verkazia)	VKC	1 drop QID in each affected eye	4 drops/day in each eye

VI. Product Availability

Drug Name	Availability
Cyclosporine ophthalmic solution (Cequa)	Single use vial: 0.09%, 0.25 mL each of 60 vials/tray
Cyclosporine ophthalmic emulsion (Restasis)	• Single use vial: 0.05%, 0.4 mL each of 30 vials/tray and 60 vials/tray • MultiDose bottle: 0.05%, 5.5 mL total

Drug Name	Availability
Cyclosporine ophthalmic emulsion (Verkazia)	Single use vial: 0.1% (1 mg/mL), 0.3 mL each of 30, 60, or 120 vials/box
Cyclosporine ophthalmic solution (Vevye)	Multiple-dose bottle: 0.1% (1 mg/mL), 2 mL total

VII. References

1. Cequa Prescribing Information. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; September 2019. Available at: www.cequapro.com. Accessed January 20, 2023.
2. Restasis Prescribing Information. Irvine, CA: Allergan, Inc.; July 2017. Available at: https://www.restasis.com. Accessed January 20, 2023.
3. Verkazia Prescribing Information. Emeryville, CA: Santen Inc; June 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214965s000lbl.pdf. Accessed January 20, 2023.
4. Vevye Prescribing Information. Irvine, CA: Novaliq; May 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/217469s000lbl.pdf. Accessed June 7, 2023.
5. The International Dry Eye Workshop. *Ocul Surf*. 2007; 5(2):65-204.
6. American Academy of Ophthalmology Cornea/External Disease Committee. Preferred Practice Pattern® Guidelines. Dry Eye Syndrome. Chicago, IL: American Academy of Ophthalmology; November 2018. Available at: www.aao.org/ppp. Accessed January 20, 2023.
7. American Academy of Ophthalmology Cornea/External Disease Committee. Preferred Practice Pattern® Guidelines. Conjunctivitis. Chicago, IL: American Academy of Ophthalmology; November 2018. Available at: www.aao.org/ppp. Accessed January 20, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2019 annual review: no significant changes; added contraindications; added examples of alternative anti-inflammatory agents; references reviewed and updated	02.06.19	05.19
Updated therapeutic alternatives table.	08.24.19	
2Q 2020 annual review: no significant changes; updated contraindications; references reviewed and updated	02.07.20	05.20
Added Cequa to policy per SDC and prior clinical guidance.	02.19.20	
Per December SDC and prior clinical guidance, removed Commercial line of business as PA no longer required.		
2Q 2021 annual review: no significant changes; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	02.15.21	05.21
RT4: added Verkazia and corresponding criteria for VKC; for all indications, added that multiple ophthalmic cyclosporine products should not be used in combination; added Commercial line of business for Verkazia with notation that the NF policy should be used	07.16.21	11.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
for Cequa and no policy is required for Restasis; per August SDC added Legacy WellCare authorization limits (retire WCG.CP.PMN.48).		
2Q 2022 annual review: per March SDC for Cequa and Restasis added requirement that member must use generic Restasis; removed legacy WellCare specific approval durations as Medicaid approval durations should be used instead; references reviewed and updated.	03.22.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.07.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	01.20.23	05.23
RT4: added new dosage form Vevye	06.07.23	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.