Clinical Policy: Ophthalmics – Anti-inflammatory/Immunomodulators (Cequa, Restasis, Restasis Multidose, Verkazia, Xiidra)

Reference Number: AZ.CP.PMN.1014
Effective Date: 08.01.19
Last Review Date: 02.22
Line of Business: Arizona Medicaid (AzCH-CCP and Care1st)

Revision Log

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

Description
The following are ophthalmics – anti-inflammatory/immunomodulators requiring prior authorization: cyclosporine (Cequa™, Restasis®, Restasis Multidose™, Verkazia®) and lifitegrast (Xiidra™).

AHCCCS preferred drugs in this class include Restasis (cyclosporine).

AHCCCS non-preferred drugs in this class include Cequa (cyclosporine), Restasis Multidose (cyclosporine), Verkazia (cyclosporine), and Xiidra (lifitegrast).

FDA approved indications
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.

Xiidra is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

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 Arizona Complete Health-Complete Care Plan and Care1st that Cequa, Restasis, Restasis Multidose, and Xiidra are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria
A. Keratoconjunctivitis Sicca/Dry Eye Disease (must meet all)**:**
1. Diagnosis of keratoconjunctivitis sicca or dry eye disease;

2. Member meets one of the following (a, b, or c):
    a. For Cequa: age ≥ 18 years;
    b. For Restasis: age ≥ 16 years;
    c. For Xiidra: age ≥ 17 years;
3. Failure of 2 artificial tear products containing different active ingredients, unless all are contraindicated or clinically significant adverse effects are experienced;
4. 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;
5. For Cequa, Restasis Multidose, or Xiidra: Failure of a trial of ≥ 3 consecutive months of **Restasis**, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed maximum dose indicated in *Section V*.

Approval duration: 6 months (Cequa, Restasis Multidose, Verkazia)
Length of Benefit (Restasis, Xiidra)

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);
7. Request does not exceed 120 vials per affected eye per 30 days.

Approval duration: 6 months

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): AZ.CP.PMN.53 for Arizona Medicaid.

II. Continued Therapy

A. Keratoconjunctivitis Sicca/Dry Eye Disease (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

2. For Cequa, Restasis Multidose or Xiidra: History of failure of a trial of ≥ 3 consecutive months of **Restasis**, unless contraindicated or clinically significant adverse effects are experienced;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed the FDA approved maximum recommended dose (*see Section V*).

Approval duration: 12 months

B. Vernal Keratoconjunctivitis (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
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);
5. If request is for a dose increase, request does not exceed 120 vials per affected eye per 30 days.

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): AZ.CP.PMN.53 for Arizona 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 – AZ.CP.PMN.53 for Arizona Medicaid.

IV. Appendices/General Information

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

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.

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
• artificial tears (e.g., Visine dry eye relief) • Refresh P.M.® (artificial tear ophthalmic ointment) • Systane® Nighttime (white petrolatum-mineral oil ophthalmic ointment) • Lacri-Lube® (artificial tears ointment)	Solution/gel: 1 to 2 drops in affected eye(s) BID or QID Ointment: Apply small amount (~1/4 inch) to the inside of the lower eyelid 1-4 times/day as needed	Varies
ophthalmic anti-inflammatory agents for keratoconjunctivitis sicca (e.g., prednisolone, dexamethasone, fluorometholone) fluorometholone ointment/suspension (FML®, FML® Forte®, FML® LiquifilmTM, Flarex®) Note: Ophthalmic NSAIDs are not indicated.	1 to 2 drops in each eye BID to QID for up to 2 weeks Ointment (FML): Apply small amount (~1/2 inch ribbon) to conjunctival sac 1-3 times daily Suspension (Flarex): 1-2 drops into conjunctival sac QID FML, FML Forte: 1 drop into conjunctival sac BID-QID	Varies
topical dual-acting mast cell stabilizer/antihistamine for VKC (e.g., azelastine, bepotastine, epinastine, ketotifen, olopatadine)	1 to 2 drops in affected eye(s) per day	Varies
topical mast cell stabilizer for VKC (e.g., cromolyn, lodoxamide, nedocromil)	2 to 6 drops in affected eye(s) per day	Varies
topical antihistamine for VKC (e.g., alcaftadine, emedastine)	1 to 4 drops in affected eye(s) per day	Varies

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

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
Cequa, Restasis, Restasis Multidose (cyclosporine)	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 (Verkazia)	VKC	1 drop QID in each affected eye	4 drops/day in each eye
Xiidra (lifitegrast)	DED	Instill 1 drop BID in each eye (~12 hours apart)	2 drops/eye/day

VI. Product Availability

Drug Name	Availability
cyclosporine (Restasis)	Single use vial: 0.05%, 0.4 mL each of 30 vials/tray and 60 vials/tray
cyclosporine (Restasis Multidose)	Multidose bottle: 0.05%, 5.5 mL total
cyclosporine (Cequa)	Single use vial: 0.09%, 0.25mL each of 10 vials/pouch and 6 pouches/box
Cyclosporine ophthalmic emulsion (Verkazia)	Single use vial: 0.1% (1 mg/mL), 0.4 mL each of 30, 60, or 120 vials/box

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Drug Name	Availability
lifitegrast (Xiidra)	Ophthalmic solution containing lifitegrast 5% (50mg/mL): 0.2mL containers (60 single-use containers/box)

VII. References
1. Cequa Prescribing Information. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; September 2019. Available at: www.cequapro.com. Accessed January 22, 2022.
2. Restasis Prescribing Information. Irvine, CA: Allergan, Inc.; March 2021. Available at: https://www.restasis.com/. Accessed January 22, 2022.
3. Xiidra Prescribing Information. Lexington, MA: Shire US Inc.; November 2020. Available at: https://www.xiidra.com. Accessed January 22, 2022.
4. Verkazia Prescribing Information. Emeryville, CA: Santen Inc; June 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/214965s000lbl.pdf. Accessed January 22, 2022.
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 22, 2022.
7. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed January 22, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.05.19	08.19
Added criterion for history of failure of preferred ophthalmics for Continued Therapy; Renumbered from AZ.CP.PMN.21 to AZ.CP.PMN.1014	10.07.19	10.19
2Q 2020 annual review: no significant changes; updated contraindications; references reviewed and updated	04.2020	04.2020
4Q 2020 annual review Xiidra; No significant changes. References reviewed and updated.	10.20.20	11.7.20
Added Care1st logo. Added verbiage to specify that criteria also applies to Care1st.	5.10.21	04.21
RT4: added Verkazia and corresponding criteria for VKC; for all indications, added that multiple ophthalmic cyclosporine products should not be used in combination; 4Q 2021 Xiidra annual review-no significant changes; Added Length of Benefit for initial and reauthorization for Restasis and Xiidra. References reviewed and updated.	10.30.21	11.21

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q Annual review. References reviewed and updated.	01.22.22	02.22

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.

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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.