Effective Date **2/1/2024**
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Coverage Policy Number **IP0027**

Ophthalmic Glaucoma Agents - Prostaglandin Analogs and Rho Kinase Inhibitors

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Related Coverage Resources

Quantity Limitations

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. 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

This policy supports medical necessity review for the following ophthalmic prostaglandin analog products:

- **Iyuzeh™** (latanoprost 0.005% ophthalmic solution) [preservative-free]
- **Lumigan®** (bimatoprost 0.01% ophthalmic solution)
- **Rhopressa®** (netarsudil 0.02% ophthalmic solution)
- **Rocklatan™** (netarsudil 0.02%/latanoprost 0.005% ophthalmic solution)
- **tafluprost 0.0015%** ophthalmic solution
- **Travatan® Z** (travoprost 0.004% ophthalmic solution)
- **Vyzulta™** (latanoprostene bunod 0.024% ophthalmic solution)
- **Xalatan®** (latanoprost 0.005% ophthalmic solution)
- **Xelpros™** (latanoprost 0.005% ophthalmic emulsion)
- **Zioptan®** (tafluprost 0.0015% ophthalmic solution)

Additional criteria that support the review for medical necessity exceptions of non-covered products are located in the Non-Covered Product Table by the respective plan type and drug list where applicable.

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

Medical Necessity Criteria

Ophthalmic Glaucoma Agents - Prostaglandin Analogs and Rho Kinase Inhibitors (Iyuzeh, Lumigan, Rhopressa, Rocklatan, tafluprost 0.0015% ophthalmic solution, Travatan Z, Vyzulta, Xalatan, Xelpros, Zioptan) are considered medically necessary when the following are met:

Reduction of Intraocular Pressure in Open-Angle Glaucoma or Ocular Hypertension. Individual meets the following criteria:

A. Non-Covered Product Criteria is met, refer to below table(s)

Employer Group Non-Covered Products Criteria:

Non-Covered Product	Criteria
Iyuzeh (latanoprost 0.005% ophthalmic solution) [preservative-free]	Documentation of **ONE** of the following: 1. Trial of **latanoprost 0.005% ophthalmic solution** (generic for **Xalatan**) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction. [BAK preservative] 2. Allergy / sensitivity to benzalkonium chloride [BAK] or other preservatives
Lumigan (bimatoprost 0.01% ophthalmic solution) Contains benzalkonium chloride (BAK) as preservative	Documented failure, contraindication, or intolerance to **TWO** of the following: 1. latanoprost 0.005% ophthalmic solution [BAK preservative] 2. travoprost 0.004% ophthalmic solution [ionic buffering system preservative, no BAK] 3. tafluprost 0.0015% ophthalmic solution [preservative-free]
Travatan Z (travoprost 0.004% ophthalmic solution) Contains sofZia™ ionic buffering system as preservative, no benzalkonium chloride (BAK)	Documentation of **BOTH** of the following: 1. Trial of **travoprost 0.004% ophthalmic solution** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction. [contains ionic buffering system preservative, no BAK] 2. Failure, contraindication, or intolerance to **ONE** of the following: A. bimatoprost 0.03% ophthalmic solution [BAK preservative] B. latanoprost 0.005% ophthalmic solution [BAK preservative] C. tafluprost 0.0015% ophthalmic solution [preservative-free]
Vyzulta (latanoprostene bunod) 0.024% Contains benzalkonium chloride (BAK) as preservative	Documented failure, contraindication, or intolerance to **TWO** of the following: 1. bimatoprost 0.03 % ophthalmic solution [BAK preservative] 2. latanoprost 0.005% ophthalmic solution [BAK preservative] 3. travoprost 0.004% ophthalmic solution [ionic buffering system preservative, no BAK] 4. tafluprost 0.0015% ophthalmic solution [preservative-free]

Non-Covered Product	Criteria
Xalatan (latanoprost 0.005% ophthalmic solution) Contains benzalkonium chloride as preservative (BAK)	Documented trial of **latanoprost 0.005% ophthalmic solution** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction. [BAK preservative]
Xelpros (latanoprost 0.005% ophthalmic emulsion) Contains potassium sorbate 0.47% as preservative, no benzalkonium chloride (BAK)	Documentation of **ONE** of the following: 1. Trial of **latanoprost 0.005% ophthalmic solution** (generic for **Xalatan**) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction. [BAK preservative] 2. Allergy / sensitivity to benzalkonium chloride [BAK]
Zioptan (tafluprost 0.0015% ophthalmic solution) Preservative-free	Documentation of **BOTH** of the following: 1. Trial of **tafluprost 0.0015% ophthalmic solution** (generic for **Zioptan**) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction. [Preservative-free] 2. Failure, contraindication, or intolerance to **ONE** of the following: A. bimatoprost 0.03 % ophthalmic solution [BAK preservative] B. latanoprost 0.005% ophthalmic solution [BAK preservative] C. travoprost 0.004% ophthalmic solution [ionic buffering system preservative, no BAK]

Individual and Family Plan Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Iyuzeh (latanoprost 0.005% ophthalmic solution) [preservative-free]	Documentation of **ONE** of the following: 1. Trial of **latanoprost 0.005% ophthalmic solution** (generic for **Xalatan**) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction. [BAK preservative] 2. Allergy / sensitivity to benzalkonium chloride [BAK] or other preservatives
Lumigan (bimatoprost 0.01% ophthalmic solution)	Documented failure, contraindication or intolerance to **TWO** of the following: 1. latanoprost 0.005% ophthalmic solution [BAK preservative] 2. travoprost 0.004% ophthalmic solution [ionic buffering system preservative, no BAK] 3. tafluprost 0.0015% ophthalmic solution [preservative-free] (may require prior authorization)

Non-Covered Product	Criteria
Contains benzalkonium chloride (BAK) as preservative	
Rhopressa (netarsudil 0.02% ophthalmic solution)	Documented failure, contraindication, or intolerance to **BOTH** of the following: 1. **ONE** prostaglandin analog (for example, bimatoprost 0.03% ophthalmic solution, bimatoprost [Lumigan] 0.01% ophthalmic solution [may require prior authorization], latanoprost [Xalatan] 0.005% ophthalmic solution, tafluprost [Zioptan] 0.0015% ophthalmic solution[may require prior authorization], travoprost [Travatan Z] 0.004% ophthalmic solution) 2. **EITHER** of the following: A. Another class of therapy (for example, ophthalmic beta-blockers, alpha agonists, parasympathomimetics, topical or oral carbonic anhydrase inhibitors) B. A second prostaglandin analog (for example, bimatoprost 0.03% ophthalmic solution, bimatoprost [Lumigan] 0.01% ophthalmic solution [may require prior authorization], latanoprost [Xalatan] 0.005% ophthalmic solution, tafluprost [Zioptan] 0.0015% ophthalmic solution[may require prior authorization], travoprost [Travatan Z] 0.004% ophthalmic solution)
Rocklatan (netarsudil 0.02%/ latanoprost 0.005% ophthalmic solution)	Documented inability to use single agents Rhopressa [may require prior authorization], AND latanoprost [Xalatan] 0.005% ophthalmic solution concurrently
tafluprost 0.0015% ophthalmic solution	**ONE** of the following: 1. Individual <u>without</u> benzalkonium chloride sensitivity, has had failure, contraindication, or is intolerant to **TWO** of the following: A. bimatoprost 0.03 % ophthalmic solution [BAK preservative] B. latanoprost 0.005% ophthalmic solution [BAK preservative] C. travoprost 0.004% ophthalmic solution [ionic buffering system preservative, no BAK] 2. Individual <u>with</u> benzalkonium chloride sensitivity has had failure, contraindication or is intolerant to travoprost 0.004% ophthalmic solution [ionic buffering system preservative, no BAK] 3. Individual has sensitivity to ophthalmic preservatives other than benzalkonium chloride (for example, potassium sorbate or ionic buffering systems like sofZia™)
Travatan Z (travoprost 0.004% ophthalmic solution) Contains sofZia™ ionic buffering system as preservative,	Documentation of **BOTH** of the following: 1. Trial of **<u>travoprost 0.004% ophthalmic solution</u>** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction. [contains ionic buffering system preservative, no BAK] 2. Failure, contraindication, or intolerance to **ONE** of the following: A. bimatoprost 0.03% ophthalmic solution [BAK preservative] B. latanoprost 0.005% ophthalmic solution [BAK preservative] C. tafluprost 0.0015% ophthalmic solution [preservative-free] (may require prior authorization)

Non-Covered Product	Criteria
no benzalkonium chloride (BAK)	
Vyzulta (latanoprostene bunod) 0.024% Contains benzalkonium chloride (BAK) as preservative	Documented failure, contraindication or intolerance to **TWO** of the following: 1. bimatoprost 0.03 % ophthalmic solution [BAK preservative] 2. latanoprost 0.005% ophthalmic solution [BAK preservative] 3. travoprost 0.004% ophthalmic solution [ionic buffering system preservative, no BAK] 4. tafluprost 0.0015% ophthalmic solution [preservative-free] (may require prior authorization)
Xalatan (latanoprost 0.005% ophthalmic solution) Contains benzalkonium chloride as preservative (BAK)	Documented trial of **latanoprost 0.005% ophthalmic solution** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction. [BAK preservative]
Xelpros (latanoprost 0.005% ophthalmic emulsion) Contains potassium sorbate 0.47% as preservative, no benzalkonium chloride (BAK)	Documentation of **ONE** of the following: 1. Trial of **latanoprost 0.005% ophthalmic solution** (generic for **Xalatan**) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction. [BAK preservative] 2. Allergy / sensitivity to benzalkonium chloride [BAK]
Zioptan (tafluprost 0.0015% ophthalmic solution) Preservative-free	Documentation of **BOTH** of the following: 1. Trial of **tafluprost 0.0015% ophthalmic solution** (generic for **Zioptan**) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction. [Preservative-free] (may require prior authorization) 2. Failure, contraindication, or intolerance to **ONE** of the following: A. bimatoprost 0.03 % ophthalmic solution [BAK preservative] B. latanoprost 0.005% ophthalmic solution [BAK preservative] C. travoprost 0.004% ophthalmic solution [ionic buffering system preservative, no BAK]

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.

Reauthorization Criteria

Continuation of Ophthalmic Prostaglandin Analogs (Iyuzeh, Lumigan, Rhopressa, Rocklatan, tafluprost 0.0015% ophthalmic solution, Travatan Z, Vyzulta, Xalatan, Xelpros, Zioptan) is considered medically necessary for the reduction of intraocular pressure in Open-Angle Glaucoma or Ocular Hypertension when the above medical necessity criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration is up to 12 months.
Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Any other use is considered not medically necessary including the following (this list may not be all inclusive):

Cosmetic Conditions (for example, eyelash growth)

Background

OVERVIEW
The ophthalmic prostaglandins, rho kinase inhibitor, and rho kinase inhibitor-prostaglandin combination products are indicated for the **reduction of elevated intraocular pressure (IOP)** in patients with open-angle glaucoma or ocular hypertension.[1-10]

Guidelines
The American Academy of Ophthalmology (AAO) Preferred Practice Pattern® guidelines (2020) for the treatment of primary open-angle glaucoma note that the initial therapy choice may be influenced by potential cost, side effects, and dosing schedules as well as the patient's comorbid conditions (e.g., asthma, chronic obstructive lung disease, cardiac arrhythmia).[11] Lowering the pretreatment IOP by 25% or more has been shown to slow progression of primary open-angle glaucoma. The prostaglandins are often selected as the initial medical therapy unless there are considerations (e.g., contraindications, cost, side effects) that would preclude its use. Moreover, the prostaglandins are the most frequently prescribed eye drops for lowering IOP due to efficacy and tolerability and they are dosed once daily. Other ophthalmic drugs for the treatment of glaucoma include beta-adrenergic blockers, alpha$_2$-adrenergic agonists, rho kinase inhibitors, and carbonic anhydrase inhibitors. If a drug fails to reduce IOP sufficiently, then either switching to an alternative medication as monotherapy or adding medication is appropriate, until the desired IOP level is attained.

Conjunctival Hyperemia
All of the agents in this class have been noted to cause conjunctival hyperemia.[1-10] While not a direct comparison, the incidences of hyperemia reported in product labeling are as follows: latanoprost (Xalatan, generics) 5% to 15%; Xelpros, ocular hyperemia, 41%, conjunctival hyperemia, 15%; Vyzulta 6%, Zioptan 4% to 20%; Lumigan 0.01% or bimatoprost 0.03%, 25% to 45%; Travatan Z, 30% to 50%; Rhopressa 53%, Rocklatan 59%. The discontinuation rates noted in the package labeling due to conjunctival hyperemia were < 1% of patients for latanoprost (Xalatan, generics), 0.5% to 3% of patients for Lumigan 0.01% or bimatoprost 0.03%, up to 3% of patients for Travatan Z, 6% of patients for Rhopressa, and 5% of patients for Rocklatan. The discontinuation rate due to ocular hyperemia was < 1% for Xelpros. The discontinuation rate due to ocular adverse events, including ocular hyperemia, conjunctival irritation, eye irritation, eye pain, conjunctival edema, blurred vision, punctate keratitis, and foreign body sensation is 0.6% for Vyzulta. A 2010 meta-analysis found the probability of hyperemia-type reactions varied between the prostaglandins, with latanoprost significantly less likely to cause hyperemia compared with Lumigan, travoprost, or their combination with timolol (mean proportion was 24%, 59%, and 47% for latanoprost [Xalatan, generics], Lumigan, and travoprost, respectively).[12]

Preservatives
Benzalkonium chloride (BAK), the most common preservative used in ophthalmic products, can have toxic effects on the cornea and conjunctiva.[13] All of the products listed in this policy are preserved with BAK except Travatan

Z, Xelpros, and Zioptan.[1-9] Travatan Z is preserved with an ionic buffered system, sofZia (boric acid, propylene glycol, sorbitol, zinc chloride).[5] Xelpros is preserved with potassium sorbate 0.47%.[8] Zioptan does not contain any preservatives.[9]

References

1. Bimatoprost 0.03% ophthalmic solution [prescribing information]. Weston, FL: Apotex; November 2020.
2. Lumigan® 0.01% ophthalmic solution [prescribing information]. Madison, NJ: Allergan; September 2020.
3. Rhopressa® [prescribing information]. Irvine, CA: Aerie Pharmaceuticals; March 2019.
4. Rocklatan [prescribing information]. Irvine, CA: Aerie Pharmaceuticals,; June 2020.
5. Travatan® Z 0.004% ophthalmic solution [prescribing information]. East Hanover, NJ: Novartis; October 2021.
6. Vyzulta™ [prescribing information]. Bridgewater, NJ: Bausch + Lomb; May 2019.
7. Xalatan® 0.005% ophthalmic solution [prescribing information]. New York, NY: Pfizer; April 2017.
8. Xelpros™ [prescribing information]. Cranbury, NJ: Sun Pharmaceutical; December 2020.
9. Zioptan® 0.0015% ophthalmic solution [prescribing information]. Lake Forest, IL: Akorn; November 2018.
10. Iyuzeh™ [prescribing information]. Lexington, MA: Thea; December 2022.
11. Gedde SJ, Vinod K, Wright MW, et al. The American Academy of Ophthalmology Primary Open-Angle Glaucoma Preferred Practice Pattern®. Available athttps://www.aaojournal.org/article/S0161-6420(20)31024-1/fulltext. Accessed on December 7, 2022.
12. Orme M, Collins S, Dakin H, et al. Mixed treatment comparison and meta-regression of the efficacy and safety of prostaglandin analogues and comparators for primary open-angle glaucoma and ocular hypertension. *Curr Med Res Opin*. 2010;26(3):511-528.
13. Mirza SK, Johnson SM. Efficacy and patient tolerability of travoprost BAK-free solution in patients with open-angle glaucoma and ocular hypertension. *Clin Ophthalmol*. 2010;4:877-888.