

brimonidine/timolol (Combigan)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

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Summary

Glaucoma is a chronic condition characterized by the damage to the optic nerve, which if left untreated, can lead to vision loss and ultimately, blindness. Often, but not always, this damage is associated with elevated intraocular pressure (IOP). There are several types of glaucoma, the most common being primary open-angle glaucoma. Angle-closure glaucoma and congenital glaucoma are typically managed by surgical intervention, while primary open-angle glaucoma is primarily managed pharmacologically. Ocular hypertension is diagnosed when one has elevated ocular pressure, without visual field loss or damage to the optic nerve. The overarching goal of treatment is to reduce IOP, which is currently the only modifiable risk factor for glaucoma. IOP reduction can be achieved by decreasing the production of aqueous humor or by increasing the outflow of this fluid from the anterior chamber of the eye. Therapeutic approaches include prostaglandins (e.g., latanoprost [Xalatan, Iyuzeh], bimatoprost [Durysta, Lumigan], travoprost [iDose TR, Travatan Z]), beta-blockers (e.g., timolol [Betimol], betaxolol [Betoptic-S]), alpha-adrenergic agonists (e.g., brimonidine [Alphagan P]), or laser therapy.

The American Academy of Ophthalmology recommends considering medication efficacy, side effects, and dosing frequency when selecting a pharmacological treatment, as these factors can significantly influence adherence to, and subsequent effectiveness of, therapy.

Brimonidine and timolol, which are combined in an ophthalmic solution (Combigan), can reduce IOP in those with open-angle glaucoma or ocular hypertension. This medication may be indicated when an individual requires adjunctive or replacement therapy due to inadequate IOP control. Brimonidine is a selective alpha-agonist and timolol is a beta-blocker, with the hypotensive effect of brimonidine being additive to timolol. The brimonidine tartrate/timolol maleate ophthalmic solution 0.2%/0.5% (Combigan) is FDA-approved for the treatment of glaucoma or ocular hypertension for topical ophthalmic use.

Definitions

“Documentation” refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

“Ocular hypertension” refers to a condition where the pressure inside the eye, known as intraocular pressure (IOP), is consistently higher than normal ranges. It's important to note that ocular hypertension does not necessarily imply damage to the optic nerve, but it is a risk factor for developing glaucoma.

“Open-angle glaucoma” is a form of glaucoma characterized by an anatomically normal angle between the iris and cornea, but a dysfunction in the eye's natural drainage system. This dysfunction leads to the build-up of fluid, increased IOP, and over time, can cause progressive damage to the optic nerve. This

condition, also known as primary or chronic glaucoma, typically develops slowly and painlessly and can lead to a gradual loss of vision if not effectively managed.

“[s]” indicates state mandates may apply.

Clinical Indications

Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

The Plan considers brimonidine/timolol (Combigan) medically necessary when ALL of the following criteria are met:

1. The member is 2 years of age or older; *AND*
2. Brimonidine/timolol (Combigan) is being prescribed at a dose and frequency that is within FDA approved labeling *OR* is supported by compendia or evidence-based published dosing guidelines for the requested indication; *AND*
3. The member meets the applicable [Medical Necessity Criteria for Initial Clinical Review](#) or [Subsequent Clinical Review](#) listed below.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Open-angle Glaucoma or Ocular Hypertension

The Plan considers brimonidine/timolol (Combigan) medically necessary when ALL of the following criteria are met:

4. The member meets the above [General Medical Necessity Criteria](#); *AND*
5. The member has a documented diagnosis of open-angle glaucoma or ocular hypertension; *AND*
6. The member is unable to use, or has tried and failed the individual components (brimonidine and timolol) as separate products taken concomitantly^[s]; *AND*
7. The member has tried and failed TWO (2) of the following drugs, each from a different class^[s]:
 - a. Prostaglandins; *and/or*
 - i. Bimatoprost; *or*
 - ii. Latanaprost; *or*
 - iii. Tafluprost; *or*
 - iv. Travoprost; *or*
 - b. Beta-blockers; *and/or*
 - i. Betaxolol Hcl; *or*
 - ii. Carteolol Hcl; *or*
 - iii. Levobunolol Hcl; *or*
 - c. Carbonic anhydrase inhibitors; *and/or*
 - i. Brinzolamide; *or*

- ii. Dorzolamide Hcl; *or*
- d. Alpha agonists; *and/or*
 - i. Apraclonidine Hcl (Iopidine); *or*
- e. Combination therapy; *and/or*
 - i. Brinzolamide/Brimonidine (Simbrinza); *or*
 - ii. Dorzolamide Hcl/Timolol maleate (Cosopt).

If the above prior authorization criteria are met, brimonidine/timolol (Combigan) will be approved for up to 12 months.^[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Open-angle Glaucoma or Ocular Hypertension

The Plan considers brimonidine/timolol (Combigan) medically necessary when ALL of the following criteria are met:

1. The member meets the above applicable [General Medical Necessity Criteria](#) and/or [Initial Clinical Review](#); *AND*
2. Recent chart documentation (within the last 12 months) shows the member has experienced a therapeutic response to the requested medication as evidenced by ONE (1) of the following:
 - a. clinical improvement in symptoms since starting the requested medication; *or*
 - b. disease stability since starting the requested medication.

[Experimental / Investigational, or unproven](#)^[s]

Brimonidine/timolol (Combigan) for any other use is considered experimental, investigational, or unproven.

References

1. Alcon. Simbrinza® (brinzolamide and brimonidine tartrate) ophthalmic suspension prescribing information. Fort Worth, TX; 2015 Nov.
2. Allergan. Combigan® (brimonidine tartrate and timolol maleate) ophthalmic solution prescribing information. Irvine, CA; 2019 Jun.
3. American Academy of Ophthalmology Glaucoma Panel. Preferred Practice Pattern® Guidelines. Primary Angle Closure. San Francisco, CA: American Academy of Ophthalmology; 2015. Available at: <https://www.aao.org/preferred-practicepattern/primary-angle-closure-ppp-2015>.
4. American Academy of Ophthalmology Glaucoma Panel. Preferred Practice Pattern® Guidelines. Primary Open-Angle Glaucoma. San Francisco, CA: American Academy of Ophthalmology; 2015. Available at: <https://www.aao.org/preferredpractice-pattern/primary-open-angle-glaucoma-ppp-2015>.
5. American Academy of Ophthalmology. Preferred Practice Pattern® Guidelines. Primary Open-Angle Glaucoma. San Francisco, CA: American Academy of Ophthalmology; 2020. Available at:

- <https://www.aao.org/education/preferred-practice-pattern/primary-open-angle-glaucoma-ppp>. Accessed 13 August 2025.
6. American Optometric Association (2024). Care of the Patient with Primary Open-Angle Glaucoma: Evidence-Based Clinical Practice Guideline. St. Louis, MO: American Optometric Association. Available at: <https://www.aao.org/a/19461>. Accessed 13 August 2025.
 7. Bausch & Lomb Pharmaceuticals, Inc. Brimonidine tartrate ophthalmic solution 0.2% prescribing information. Bridgewater, NJ; 2018 Nov.
 8. Bausch & Lomb. Lumify® (brimonidine tartrate) ophthalmic solution drug facts. Bridgewater, NJ; Undated.
 9. Boyd K. What is Glaucoma? American Academy of Ophthalmology. Last Updated Sept 2021. Accessed Sept 2021. Available at: <https://www.aao.org/eye-health/diseases/what-is-glaucoma>.
 10. Boyd K. What is Ocular Hypertension? American Academy of Ophthalmology. Last Updated Mar 2021. Accessed Sept 2021. Available at: <https://www.aao.org/eye-health/diseases/what-is-ocular-hypertension>.
 11. Clinical Pharmacology [database on the Internet]. Tampa (FL): Elsevier Inc.: 2022. Available from: www.clinicalpharmacology.com. Updated periodically. Accessed: May, 2022.
 12. Combigan (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5% [prescribing information]. Allergan, Inc: Irvine, CA. October 2015.
 13. DailyMed. Package Inserts. U.S. National Library of Medicine, a National Institutes of Health (NIH) website. Accessed May, 2022. <https://dailymed.nlm.nih.gov/dailymed/index.cfm>.
 14. Gedde SJ, Lind JT, Wright MM, Chen PP, Muir KW, Vinod K, Li T, Mansberger SL; American Academy of Ophthalmology Preferred Practice Pattern Glaucoma Panel. Primary Open-Angle Glaucoma Suspect Preferred Practice Pattern®. Ophthalmology. 2021 Jan;128(1):P151-P192. doi: 10.1016/j.ophtha.2020.10.023. Epub 2020 Nov 12. PMID: 34933743.
 15. Gedde SJ, Vinod K, Wright MW, et al. Primary open-angle glaucoma Preferred Practice Pattern guidelines. The American Academy of Ophthalmology. 2020. Available at: <http://www.aao.org/guidelinesbrowse>.
 16. Glaucoma Research Foundation. Open-Angle Glaucoma. Last updated Dec 2019. Accessed Sept 2021. Available at: <https://www.glaucoma.org/glaucoma/symptoms-of-primary-open-angle-glaucoma.php>
 17. Gupta D, Chen PP. Glaucoma. Am Fam Physician. 2016; 93:668-74.
 18. Kerr N. Combination Brimonidine and Timolol. Ophthalmology. 2010 January; 117(1): 193. <Indicates that peripheral skin necrosis is a potential complication of Combigan>
 19. Lexicomp Online Database [database on the Internet]. Hudson (OH): Lexicomp Inc.: 2022. Available from: <http://online.lexi.com>. Updated periodically. Accessed: May, 2022.
 20. Li T, Lindsley K, Rouse B, et al. Comparative Effectiveness of First-Line Medications for Primary Open-Angle Glaucoma: A Systematic Review and Network Meta-analysis. Ophthalmology. 2016 Jan;123(1):129-40. doi: 10.1016/j.ophtha.2015.09.005. Epub 2015 Oct 31.
 21. Liebmann JM, Lee JK. Current therapeutic options and treatments in development for the management of primary open-angle glaucoma. Am J Manag Care. 2017; 23(15 Suppl):S279-S292.
 22. Micromedex Solutions [database on the Internet]. Greenwood Village, CO: Truven Health Analytics: 2022. Available from: <http://micromedex.com/>. Updated periodically. Accessed: May, 2022.
 23. National Institute for Health and Care Excellence (NICE). Glaucoma: diagnosis and management. 2022 Jan 26. NICE guideline, No. 81. Available at: <https://www.nice.org.uk/guidance/ng81>. Accessed 13 August 2025.
 24. Prum BE Jr, Rosenberg LF, Gedde SJ et al. Primary open-angle glaucoma preferred practice pattern® guideline [published corrigendum appears in Ophthalmology. 2018; 125: 949]. San Francisco, CA: American Academy of Ophthalmology; 2015. From the American Academy of Ophthalmology website.
 25. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. JAMA. 2014; 311:1901-11.

Clinical Guideline Revision / History Information

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