

Allergan Glaucoma Product Portfolio Fact Sheet

Glaucoma, a group of eye diseases characterized by damage to the optic nerve, is the leading cause of preventable blindness in the United States.¹ It is estimated that three million Americans have glaucoma, but only half of those know they have it.² The total number of glaucoma cases worldwide is estimated to be 65 million.² One of the risk factors of glaucoma is elevated intraocular pressure (IOP), or pressure inside the eye. A healthy eye produces fluids, called aqueous humor, at the same rate fluids are drained. If the aqueous humor is not removed rapidly enough or the eye fills too rapidly, pressure builds up in the eye, which can result in glaucoma. This high pressure distorts the shape and damages the optic nerve. Maintaining healthy IOP levels may slow the progression of the disease and help prevent loss of vision.

Allergan Glaucoma Product Portfolio

Allergan's robust glaucoma portfolio helps eye care professionals manage their patients' elevated IOP, which may help to reduce risk of vision loss due to glaucoma. The portfolio includes industry-leading products: LUMIGAN[®] (bimatoprost ophthalmic solution) 0.03%, ALPHAGAN[®] P (brimonidine tartrate ophthalmic solution) 0.1% and 0.15%, and COMBIGAN[™] (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5%. Built on a nearly 60-year heritage in ophthalmology with expertise in discovering and developing new therapeutic agents to preserve and protect vision, Allergan is a global leader in eye care.

LUMIGAN[®] (bimatoprost ophthalmic solution) 0.03%

- LUMIGAN[®] was originally approved by the U.S. Food and Drug Administration (FDA) in 2001 for the reduction of elevated IOP in patients with open-angle glaucoma or ocular hypertension who are intolerant or insufficiently responsive to other IOP-lowering medications. In 2006, LUMIGAN[®] was approved by the FDA as a first-line treatment for elevated IOP associated with open-angle glaucoma or ocular hypertension and is now used as an initial treatment in an increasing number of patients. LUMIGAN[®] monotherapy delivers effective and sustained IOP lowering.^{3,4}
- LUMIGAN[®] ophthalmic solution offers an easy once-a-day dosing regimen. Maintaining once-daily dosing can be convenient for patients.⁵
- LUMIGAN[®] has broad formulary and Medicare Part D coverage.⁶
- LUMIGAN[®] ophthalmic solution has been reported to cause darkening (pigmentation) of eye color, eyelid skin and eyelashes, as well as increased growth of eyelashes. Pigmentation changes can increase as long as LUMIGAN[®] is used. After stopping LUMIGAN[®], darkening of eye color is likely to be permanent while darkening of the eyelid skin and eyelash changes may be reversible. The effects of increased darkening beyond five years are not known. When only one eye is treated, there is a possibility of eyelash changes in the eye treated with LUMIGAN[®] ophthalmic solution. These changes may result in differences between the eyes in eyelash length, thickness, darkness, number of eyelashes and/or direction of eyelash growth. The most common side effects of LUMIGAN[®] ophthalmic solution are eye redness, growth of eyelashes and itchy eyes.
- For more information about LUMIGAN[®] ophthalmic solution, please refer to the [full prescribing information](#) and the product Web site at www.lumigan.com.



ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1% and 0.15%

- The No. 1 branded adjunct to a lipid,⁷ the ALPHAGAN® franchise has been a leading group of therapies for reducing IOP in patients with open-angle glaucoma or ocular hypertension safely and effectively for more than five years.
- Many glaucoma patients have co-existing systemic disorders.⁸ ALPHAGAN® P 0.1% which was approved by the U.S. FDA in 2005, offers a favorable safety profile with no cardiopulmonary contraindications and no label warning or precautions regarding patients with diabetes, sexual dysfunction and obstructive pulmonary disease. ALPHAGAN® P 0.1% and 0.15% should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension or thromboangiitis obliterans.
- ALPHAGAN® P ophthalmic solution 0.1% is an improved formulation of the original ALPHAGAN® 0.2% and ALPHAGAN® P 0.15%. With ALPHAGAN® P 0.1%, the drug concentration from the original product, ALPHAGAN® 0.2% has been decreased by 50 percent without sacrificing efficacy.
- ALPHAGAN® P 0.1% and 0.15% solutions contain PURITE®, a gentle-to-the-eye preservative used in other Allergan products.
- ALPHAGAN® P 0.1% and 0.15% are contraindicated in patients receiving monoamine oxidase inhibitor therapy. Although ALPHAGAN® P 0.1% and 0.15% ophthalmic solutions had minimal effect on the blood pressure of patients in clinical studies, caution should be exercised in treating patients with severe cardiovascular disease. Adverse events associated with ALPHAGAN® P 0.1% and 0.15% occurring in approximately 10 to 20 percent of patients included allergic conjunctivitis, conjunctival hyperemia and eye pruritus.
- For more information about ALPHAGAN® P ophthalmic solution, please refer to the [full prescribing information](#) and the product Web site at www.alphaganp.com.



COMBIGAN™ (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5%

- COMBIGAN™, approved by the U.S. FDA in 2007, is an alpha adrenergic receptor agonist with a beta adrenergic receptor inhibitor indicated for the reduction of elevated intraocular pressure (IOP) in patients with glaucoma or ocular hypertension who require adjunctive or replacement therapy due to inadequately controlled IOP. The IOP-lowering of COMBIGAN™ ophthalmic solution dosed twice a day was slightly less than that seen with the concomitant administration of timolol maleate ophthalmic solution, 0.5% dosed twice a day and brimonidine tartrate ophthalmic solution, 0.2% dosed three times per day.⁹
- COMBIGAN™ ophthalmic solution offers eye care professionals an effective and well-tolerated adjunctive therapy for patients who require additional IOP lowering.
- Clinical data indicates that COMBIGAN™ ophthalmic solution is an effective adjunct to a prostaglandin analogue¹⁰ and an effective next step for beta-blocker patients who require additional IOP reduction.¹¹
- Results from pooled three-month studies found that COMBIGAN™ ophthalmic solution reduced mean IOP to 15.6 mm Hg versus a reduction to 17.2 mm Hg with *Cosopt*® at three months (demonstrated in 101 patients).¹⁰ Also, COMBIGAN™ demonstrated low burning and stinging, and 91 percent of patients reported that COMBIGAN™ was comfortable or very comfortable (demonstrated in 85 patients).¹²



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- COMBIGAN™ ophthalmic solution provides a dual mechanism of action to lower IOP.⁹ Many patients require more than one medication to meet their target IOP. COMBIGAN™ ophthalmic solution offers the IOP-lowering efficacy of two proven agents in the convenience of one bottle.
- In the 12-month pivotal trials of 1,159 patients, COMBIGAN™ ophthalmic solution significantly reduced mean IOP up to 33 percent (7.6 mm Hg) from baseline and was well tolerated with a low ocular allergy rate of 5.2 percent (demonstrated in 385 patients).¹³
- **Contraindications:** COMBIGAN™ ophthalmic solution is contraindicated in patients with bronchial asthma, a history of bronchial asthma, severe chronic obstructive pulmonary disease; in patients with sinus bradycardia, second or third degree atrioventricular block, overt cardiac failure, cardiogenic shock; and in patients with hypersensitivity to any component of this product.
- **Warnings and Precautions:** Severe respiratory reactions including death due to bronchospasm in patients with asthma have been reported following systemic or ophthalmic administration of timolol maleate. Sympathetic stimulation may be essential in individuals with diminished myocardial contractility, and its inhibition by beta-adrenergic receptor blockade may precipitate more severe cardiac failure. In patients without a history of cardiac failure, continued depression of the myocardium with beta-blocking agents over a period of time can, in some cases, lead to cardiac failure. Patients with chronic obstructive pulmonary disease (e.g., chronic bronchitis, emphysema) of mild or moderate severity, bronchospastic disease, or a history of bronchospastic disease should, in general, not receive beta-blocking agents, including COMBIGAN™. COMBIGAN™ may potentiate syndromes associated with vascular insufficiency. While taking beta-blockers, patients may be more reactive to allergens. Beta-adrenergic blockade has been reported to potentiate muscle weakness consistent with certain myasthenic symptoms. Beta-adrenergic receptor blocking agents may mask hypoglycemic symptoms in patients with diabetes mellitus. Beta-adrenergic blocking agents may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Patients suspected of developing thyrotoxicosis should be managed carefully to avoid abrupt withdrawal of beta-adrenergic blocking agents that might precipitate a thyroid storm.
- **Adverse reactions:** The most common adverse reactions occurring in approximately 5 to 15% of patients included allergic conjunctivitis, conjunctival folliculosis, conjunctival hyperemia, eye pruritus, and ocular burning and stinging.
- **Drug interactions:** Antihypertensives/cardiac glycosides may lower blood pressure. Concomitant use with systemic beta-blockers may potentiate systemic beta blockade. Oral or intravenous calcium antagonists may cause atrioventricular conduction disturbances, left ventricular failure, and hypotension. Catecholamine-depleting drugs may have additive effects and produce hypotension and/or marked bradycardia. Use with CNS depressants may result in an additive or potentiating effect. Digitalis and calcium antagonists may have additive effects in prolonging atrioventricular conduction time. CYP2D6 inhibitors may potentiate systemic beta-blockade. Tricyclic antidepressants may potentially blunt the hypotensive effect of systemic clonidine. Monoamine oxidase inhibitors may result in increased hypotension.
- For more information about COMBIGAN™ ophthalmic solution, please refer to the full prescribing information and the product Web site at www.combigan.com.

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Additional Information

For a complete list of products in the Allergan eye care portfolio and further information on each product, please visit www.allergan.com.

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¹ The Glaucoma Foundation. "TGF Urges Eye Exams to Detect the Disease Early" January 8, 2006. Available at: http://www.glaucomafoundation.org/news_story.php?i=38. Accessed April 19, 2007.

² Glaucoma Research Foundation. "Glaucoma Facts and Stats" Available at: http://www.glaucoma.org/learn/glaucoma_facts.html. Accessed July 31, 2007.

³ Noecker RS, Dirks MS, Choplin NT, et al. A six-month randomized clinical trial comparing the intraocular pressure-lowering efficacy of bimatoprost and latanoprost in patients with ocular hypertension or glaucoma. *Amer J Ophthalmol* 2003; 135(1):55-63.

⁴ Higginbotham EJ, Schuman JS, Goldberg I, et al, for the Bimatoprost Study Groups 1 and 2. One-year, randomized study comparing bimatoprost and timolol in glaucoma and ocular hypertension. *Arch Ophthalmol*. 2002; 120(10):1286-1293.

⁵ Mansukani SS. Improving adherence to drug-treatment regimens for glaucoma. *P&T Digest*. November 29, 2003; 49-53.

⁶ Pinsonault. Formulary Position by Product. August 2007.

⁷ Verispan LLC. *Physician Drug and Diagnosis Audit*. Yardley, Pa: Verispan LLC; 2006. Letter dated April 9, 2007.

⁸ Gottfredsdottir MS, Allingham RR, Shieds MB. Physicians' guide to interactions between glaucoma and systemic medications. *J Glaucoma*. 1997; 6(6):377-383.

⁹ COMBIGAN™ prescribing information.

¹⁰ Nixon D. Evaluation of the Tolerability and Efficacy of Brimonidine Tartrate 0.2% - Timolol Maleate 0.5% Ophthalmic Solution (COMBIGAN™) and Dorzolamide Hydrochloride 2% - Timolol Maleate 0.5% Ophthalmic Solution (Cosopt®) in Patients with Open-Angle Glaucoma or Ocular Hypertension. Poster presented at: 17th Annual Meeting of the American Glaucoma Society; March 1-4, 2007, San Francisco.

¹¹ Goni FJ and the Brimonidine/Timolol Fixed Combination Study Group. 12-week study comparing the fixed combination of brimonidine and timolol with concomitant use of the individual components in patients with glaucoma and ocular hypertension. *Eur J Ophthalmol*. 2005;15(5):581-590.

¹² Nixon Dr, Hollander DA. Comparison of the efficacy and tolerability of twice-daily COMBIGAN™ versus Cospot® fixed-combination therapies. Poster presented at the 111th Annual Meeting of the American Academy of Ophthalmology; November 10-13, 2007; New Orleans, LA.

¹³ Sherwood MB, Craven ER, Chou C, et al. Twice-daily 0.2% brimonidine-0.5%/timolol fixed-combination therapy vs. monotherapy with timolol or brimonidine in patients with glaucoma and ocular hypertension: a 12-month randomized trial. *Arch Ophthalmol*. 2006; 124(9): 1230-1238.