A patient’s guide to COMBIGAN®

**Indication:** COMBIGAN® (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5% is approved for reducing elevated intraocular pressure (IOP) in patients with glaucoma who require additional or adjunctive IOP lowering therapy. COMBIGAN® lowers IOP slightly less than taking both brimonidine tartrate three times a day and timolol maleate two times a day.

**IMPORTANT SAFETY INFORMATION**

**Contraindications:** COMBIGAN® ophthalmic solution should not be used by patients who have, or ever had bronchial asthma, chronic bronchitis, emphysema, slow heartbeat, impaired conduction of the heart, heart failure, or impaired pumping of the heart.

Please see additional Important Safety Information inside.
IMPORTANT SAFETY INFORMATION (continued)

Contraindications (continued): COMBIGAN® (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5% should not be used in patients under the age of 2 years, or by patients with hypersensitivity to any ingredient of this product.

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions: Severe respiratory reactions including death due to difficulty breathing have been reported in patients with asthma. Stimulation of the nervous system may be essential in individuals with diminished heart pumping ability. In patients without a history of cardiac failure, continued use of beta-blocking agents over a period of time can, in some cases, lead to cardiac failure.

All about high eye pressure and COMBIGAN®

This brochure will help you learn more about how COMBIGAN® may help to reduce high eye pressure, also known as intraocular pressure (IOP), for people who have open-angle glaucoma or ocular hypertension.

We hope that you will find this information useful. If you have any questions, please discuss them with your physician.
Why is eye pressure important?

A number of factors may contribute to open-angle glaucoma, but high pressure inside the eye, also known as high intraocular pressure (IOP), plays a very important role.

- Your eyes contain fluid that keeps them nourished and healthy
- Normally, this fluid flows within the eye and drains freely
- In people who have open-angle glaucoma, the fluid does not drain properly
- The buildup of fluid causes pressure inside the eye to rise
- If the pressure remains high for a long time, it can slowly cause damage to the optic nerve, potentially leading to glaucoma-related vision loss
- The higher the eye pressure becomes, the greater the risk for optic nerve damage and vision loss

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued): Patients with mild or moderate chronic bronchitis, emphysema, or asthma should not take COMBIGAN® (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5%. COMBIGAN® may worsen symptoms associated with poor circulation. COMBIGAN® patients who have allergies may experience stronger allergy symptoms than they would without COMBIGAN® ophthalmic solution.

Please see additional Important Safety Information on following pages.
What is COMBIGAN®?

About 2.7 million people (aged 40 and older) in the United States have open-angle glaucoma.¹ Twice-daily COMBIGAN® (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5% is a medication proven to effectively lower IOP for patients who require additional or adjunctive IOP-lowering therapy. COMBIGAN® lowers IOP slightly less than both brimonidine tartrate taken 3 times a day and timolol maleate taken 2 times a day.¹

COMBIGAN® combines 2 treatments (active ingredients)—brimonidine and timolol—in 1 bottle. Instead of prescribing these 2 medications separately, your physician has chosen to prescribe COMBIGAN®.

Why did my physician prescribe COMBIGAN® for me?

COMBIGAN® is specifically approved to lower high or elevated pressure in the eyes of people with primary open-angle glaucoma or ocular hypertension (both conditions involve elevated pressure in the eye) who require additional or adjunctive IOP-lowering therapy.¹

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued): COMBIGAN® may mask certain clinical signs of hyperthyroidism, such as rapid heartbeat. Patients with overactive thyroid who withdraw too abruptly from COMBIGAN® may experience severe hyperthyroid symptoms.

Please see additional Important Safety Information on following pages.
How does COMBIGAN® (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5% work?

COMBIGAN® is believed to work in 2 different ways1,*:

1. It decreases the amount of fluid produced in the eye.
2. It increases fluid that flows out of the eye.

Is COMBIGAN® the same thing as taking brimonidine and timolol (the 2 treatments in COMBIGAN®), separately?

No, COMBIGAN® is a specially formulated combination of these 2 treatments for reducing elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension who require additional or adjunctive IOP-lowering therapy. COMBIGAN® lowers IOP slightly less than both brimonidine tartrate taken 3 times a day and timolol maleate taken 2 times a day.

In a clinical study of 385 patients taking COMBIGAN®, 5.2% (20 out of 385 of them) experienced allergic conjunctivitis.4

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued): Ocular hypersensitivity reactions have been reported with brimonidine tartrate ophthalmic solutions 0.2%, with some reported to be associated with an increase in intraocular pressure. There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products.

Please see additional Important Safety Information on following pages.

*The exact way COMBIGAN® may work is not known.
IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued): Beta-adrenergic receptor blockade impairs the ability of the heart to respond to general anesthesia in surgical procedures and some patients have experienced protracted severe hypotension during anesthesia. In patients undergoing elective surgery, gradual withdrawal of beta-adrenergic receptor blocking agents may be recommended.

How much does COMBIGAN® cost?
The cost of COMBIGAN® will be determined by your health plan.
Be sure to ask your eye care professional about available offers and rebates.

How will I know if COMBIGAN® is working?
Only your physician can test how well this medicine is working. It is important to follow up and make appointments to have your eye pressure checked as your physician instructs.

IMPORTANT SAFETY INFORMATION (continued)

Adverse reactions: The most common adverse reactions occurring in approximately 5% to 15% of patients included allergic inflammation of the eye, abnormally large lymph follicles in the mucous membrane lining the inner surface of the eyelid and the exposed surface of the eyeball (also called the conjunctiva), eye redness, severe itching of the eyes, and burning and stinging of the eyes.

Please see additional Important Safety Information on following pages.
How often should I take COMBIGAN® (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5%?

It is recommended that patients put 1 drop of COMBIGAN® in the affected eye(s) twice daily, 12 hours apart.¹

Follow these 5 steps:

1. Wash your hands. Tilt your head back and look at the ceiling.

2. Using your index finger, gently pull down your lower eyelid to form a pocket.

3. Gently squeeze 1 drop into the pocket. Do not let the bottle tip touch your eye, your fingers, or anything else.

What to do if you wear contact lenses

COMBIGAN® (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5% contains a preservative that may be absorbed by contact lenses. If you wear contact lenses, remove them first, then wait 15 minutes after using COMBIGAN® ophthalmic solution before you put them back into your eyes.¹

What to do if you take more than 1 type of eyedrop

If you take other eyedrops besides COMBIGAN® ophthalmic solution, they should be administered at least 5 minutes apart.¹

Gently close your eyes and lightly press on the inside corners of your eyes.

Then carefully blot away any excess liquid that may be on your skin.

IMPORTANT SAFETY INFORMATION

Drug interactions: Blood pressure drugs and drugs that are used to stimulate the heart in cases of heart failure (also called cardiac glycosides) may lower blood pressure. Using COMBIGAN® ophthalmic solution together with beta-blocker drugs may interrupt beta-receptor activity (beta-blockade) within the body.

Please see additional Important Safety Information on following pages.
How to handle your COMBIGAN® (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5% bottle

It is very important to handle your COMBIGAN® bottle carefully. Always wash your hands before putting the drops in your eyes. Don’t allow anything to touch the tip—not even your eyes or the areas around your eyes! Potentially harmful bacteria may enter the bottle and cause serious eye infections. Always replace the cap after using. If you think your COMBIGAN® bottle has become contaminated, contact your eye care professional.

Why is it important to take COMBIGAN® every day?

Even if you feel fine, it’s important to continue using your COMBIGAN® eyedrops every day as your doctor prescribed. Do not skip or stop treatment before speaking with your doctor. Using COMBIGAN® may help lower your high eye pressure. Make it part of your daily routine.

Follow some helpful tips to remember to take your eyedrops:

• Associate using your eyedrops with other daily routines you’ve established for yourself, such as brushing your teeth
• Set a daily clock or watch alarm that can remind you to use your eyedrops
• Ask a friend or family member to remind you when it’s time to use your eyedrops

IMPORTANT SAFETY INFORMATION (continued)

Drug interactions (continued): Oral or intravenous calcium channel blockers that prevent calcium from entering the cells of the heart and blood vessels (calcium antagonists) may cause disturbances in the passage of blood through the heart, and/or abnormally low blood pressure.

Please see additional Important Safety Information on following pages.
Open-angle glaucoma is a lifelong disease

Open-angle glaucoma is a lifelong disease, which means treatment is also lifelong. Remembering to take your eyedrops is easier if you make them another part of your daily routine. Committing to taking your IOP-lowering medication exactly as prescribed is a way to help lower high eye pressure.

If anything interferes with your ability to take your medicine as prescribed—such as too many eyedrops to manage in your daily routine—be sure to talk to your eye care professional.

Will COMBIGAN® cure my open-angle glaucoma?

No. There is no cure for open-angle glaucoma. It is a chronic disease, but taking your eye medication as prescribed is one of the things you can do to help lower eye pressure.

IMPORTANT SAFETY INFORMATION (continued)

Drug interactions (continued): Using COMBIGAN® with digitalis, a cardiac stimulant, may have added effects in prolonging the time it takes for blood to pass through the heart. CYP2D6 inhibitors may enhance the effect of beta-blockade within the body.

Please see additional Important Safety Information on following pages.

IMPORTANT SAFETY INFORMATION (continued)

Drug interactions (continued): Drugs that significantly decrease fluids of the adrenal gland may produce low blood pressure and/or a noticeably slow heartbeat rate below 60 beats per minute. Using COMBIGAN® (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5% with central nervous system depressants may result in an increased effect.
You play an important part in your treatment

The success of your therapy ultimately depends on you and your ongoing daily commitment to taking your medication as your doctor prescribed.

What should I expect with COMBIGNAN® (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5% therapy?

Large clinical studies have shown that COMBIGNAN® is effective for reducing high eye pressure in patients with open-angle glaucoma and ocular hypertension. In 5% to 15% of 385 patients, the following adverse events were reported1,4:

• Eye allergies and inflammation • Redness of the eyes
• Itchiness or burning sensation in the eyes • Stinging

COMBIGNAN® eyedrops can be absorbed by your body. Contact your eye care professional right away if you experience any of the following potential serious side effects1:

• Shortness of breath • Visual changes
• Irregular heartbeat and/or slowing of your heart rate

COMBIGNAN® ophthalmic solution may cause fatigue and/or drowsiness. If you drive or perform hazardous work, such as operating machinery, make sure you feel appropriately alert. Ocular hypersensitivity reactions have been reported with COMBIGNAN®, with some reported to be associated with an increase in intraocular pressure. These are not the only risks associated with COMBIGNAN®. If you experience these or other side effects, you should immediately contact your eye doctor.1

IMPORTANT SAFETY INFORMATION (continued)

Drug interactions (continued): Tricyclic antidepressants may reduce the ability of clonidine to lower blood pressure. Monoamine oxidase inhibitors (a type of antidepressant drug) may result in low blood pressure.

Please see full Prescribing Information inserted in the pocket at the end of this brochure.
Who should NOT use COMBIGAN®?

COMBIGAN® should not be used if you are currently taking a type of antidepressant called an “MAO inhibitor” or if you¹:

• Have bronchial asthma or a history of bronchial asthma
• Have severe lung problems
• Have slow or irregular heartbeat or heart failure
• Have allergies to any of the ingredients in COMBIGAN®
• Are under the age of 2 years old

COMBIGAN® eyedrops can be absorbed by your body, which may be of concern if you have other medical conditions or are taking other drugs.

So tell your doctor about your other medications, especially¹:

• Heart or blood pressure medicines, such as beta-blockers and calcium channel blockers
• Sedatives • Antidepressants

It is also very important to tell your doctor if you have¹:

• Diabetes • Thyroid problems • Liver or kidney disease
• Depression • Eye injury or infection
• Upcoming surgery for your eyes or anywhere on your body

These risks are not the only risks associated with COMBIGAN®. If you experience these or other side effects, you should immediately contact your eye care professional.
Visit www.Combigan.com for more information about COMBIGAN® and to download a cost-saving rebate.

1. COMBIGAN® Prescribing Information.
4. Sherwood MB, Craven ER, Chou C, et al; for COMBIGAN® Study Groups I and II. Twice-daily 0.2% brimonidine-0.5% timolol fixed-combination therapy vs monotherapy with timolol or brimonidine in patients with glaucoma or ocular hypertension: a 12-month randomized trial. Arch Ophthalmol. 2006;124(9):1230-1238.