BETIMOL® is indicated in the treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma.

SELECT IMPORTANT SAFETY INFORMATION

BETIMOL® is contraindicated in patients with overt heart failure, cardiogenic shock, sinus bradycardia, second- or third-degree atrioventricular block, bronchial asthma or history of bronchial asthma, or severe chronic obstructive pulmonary disease, or hypersensitivity to any component of this product.

The most frequently reported ocular event in clinical trials was burning/stinging on instillation and was comparable between Betimol® and timolol maleate (approximately one in eight patients).

Please refer to the Full Prescribing Information in the top pocket for complete safety information (Contraindications, Warnings, Precautions, and Adverse Reactions) and the use of BETIMOL®.
**Start with BETIMOL®**

For your patients who may benefit from monotherapy with a beta-blocker

- Dosed 1 drop BID or QD*
- By Month 3, BETIMOL® alone delivered a 23% reduction in mean IOP compared to baseline4
- Sustained efficacy over 12 months of dosing with BETIMOL®5

**Add BETIMOL®**

When your patients need adjunctive IOP lowering

- BETIMOL® added to Xalatan® yielded a 16% reduction in mean IOP compared to baseline3**

* Upon IOP control.

** Drugs should be administered at least 5 minutes apart. The concomitant use of 2 topical beta-adrenergic blocking agents is not recommended.

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**CONTRAINDICATIONS** Betimol® is contraindicated in patients with overt heart failure, cardiogenic shock, sinus bradycardia, second- or third-degree atrioventricular block, bronchial asthma or history of bronchial asthma, or severe chronic obstructive pulmonary disease, or hypersensitivity to any component of this product.

**WARNINGS** As with other topically applied ophthalmic drugs, Betimol® is absorbed systemically. The same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. For example, severe respiratory and cardiac reactions, including death due to bronchospasm in patients with asthma, and rarely, death in association with cardiac failure have been reported following systemic or topical administration of beta-adrenergic blocking agents.

Cardiac Failure: Sympathetic stimulation may be essential for support of the circulation 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. Betimol® should be discontinued at the first sign or symptom of cardiac failure.

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BETIMOL® (timolol ophthalmic solution) 0.25%, 0.5%

**Patient comfort**
- In a published study, patients reported less burning and stinging with BETIMOL® than with Istalol®.
- Low incidence of stinging/burning (approximately 1 in 8 patients).
- A study suggests that timolol maleate may have more of an irritant effect on the corneal and nasal conjunctival epithelium.

**BETIMOL® is associated with less anterior segment side effects including stinging, burning or blurred vision**
- Maleate salt may contribute to anterior segment surface changes that can limit tolerability.
- Studies have noted that side effects may reduce compliance.

**SELECT IMPORTANT SAFETY INFORMATION**

**WARNINGS**

Obstructive Pulmonary Disease: Patients with chronic obstructive pulmonary disease (e.g. chronic bronchitis, emphysema) of mild or moderate severity, bronchospastic disease, or a history of bronchospastic disease (other than bronchial asthma or a history of bronchial asthma which are contraindications) should in general not receive beta-blocking agents.

Major Surgery: The necessity or desirability of withdrawal of beta-adrenergic blocking agents prior to a major surgery is controversial. Beta-adrenergic receptor blockade impairs the ability of the heart to respond to beta-adrenergically mediated reflex stimuli. This may augment the risk of general anesthesia in surgical procedures. Some patients receiving beta-adrenergic receptor blocking agents have been subject to protracted severe hypotension during anesthesia. Difficulty in restarting and maintaining the heartbeat has also been reported. For these reasons, in patients undergoing elective surgery, gradual withdrawal of beta-adrenergic receptor blocking agents is recommended. If necessary during surgery, the effects of beta-adrenergic blocking agents may be reversed by sufficient doses of beta-adrenergic agonists.

Diabetes Mellitus: Beta-adrenergic blocking agents should be administered with caution in patients subject to spontaneous hypoglycemia or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycemic agents. Beta-adrenergic receptor blocking agents may mask the signs and symptoms of acute hypoglycemia.

Thyrotoxicosis: 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 which might precipitate a thyroid storm.

**PRECAUTIONS**

**Pregnancy Teratogenic effects:** There are no adequate and well-controlled studies in pregnant women. Betimol® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Nursing mothers:** Because of the potential for serious adverse reactions in nursing infants from timolol, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

**Pediatric use:** Safety and efficacy in pediatric patients have not been established.

**ADVERSE REACTIONS**

The most frequently reported ocular event in clinical trials was burning/stinging on instillation and was comparable between Betimol® and timolol maleate (approximately one in eight patients).

The following adverse events were associated with use of Betimol® in frequencies of more than 5% in two controlled, double-masked clinical studies in which 184 patients received 0.25% or 0.5% Betimol®: dry eyes, itching, foreign body sensation, discomfort in the eye, eyelid erythema, conjunctival injection, and headache.

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The Benefits That Matter

- As monotherapy, BETIMOL® provides proven efficacy for consistent IOP control\(^4\)
- As adjunctive therapy, BETIMOL® delivers significant reduction in IOP levels when added to Xalatan\(^\circ\); \[P<0.001\]\(^3\)
- Less post-installation blurred vision than timolol gel solution\(^2,7\)
- Patients reported less stinging and burning compared to Istatol\(^\circ\)\(^2\)

Prescribe BETIMOL®

Comfortable and effective IOP control for your patients

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References:
2. Sonty S, Mundorf TK, Stewart JA, Stewart WC. Short-term tolerability of once-daily timolol hemihydrate 0.5%, timolol maleate in sorbate 0.5%, and generic timolol maleate gel-forming solution 0.5% in glaucoma and/or ocular hypertension: a prospective, randomized, double-masked, active-controlled, three-period crossover pilot study. Clinical Therapeutics. 2009;31:2063-2071.

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BETIMOL is a registered trademark of Oak Pharmaceuticals, Inc. All other trademarks are the property of their respective owners.
Clinical Studies
In two controlled multicenter studies in the U.S., Betimol® 0.25% and 0.5% were compared with respective timolol maleate eye drops. In these studies, the efficacy and safety profile of Betimol® was similar to that of timolol maleate.

INDICATIONS AND USAGE
Betimol® is indicated in the treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma.

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Precautions
General
Because of the potential effects of beta-adrenergic blocking agents relative to blood pressure and pulse, these agents should be used with caution in patients with cerebrovascular insufficiency. If signs or symptoms suggesting reduced cerebral blood flow develop following initiation of therapy with Betimol®, alternative therapy should be considered.

There have been reports of bacterial keratitis associated with the use of multiple dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface. (See PRECAUTIONS, Information for Patients.)

Muscle Weakness: Beta-adrenergic blockade has been reported to potentiate muscle weakness consistent with certain myasthenic symptoms (e.g. diplopia, ptosis, and generalized weakness). Beta-adrenergic blocking agents have been reported rarely to increase muscle weakness in some patients with myasthenia gravis or myasthenic symptoms.

In angle-closure glaucoma, the goal of the treatment is to reopen the angle. This requires constricting the pupil. Betimol® has no effect on the pupil. Therefore, if timolol is used in angle-closure glaucoma, it should always be combined with a miotic and not used alone.

Anaphylaxis: While taking beta-blockers, patients with a history of atopy or a history of severe anaphylactic reactions to a variety of allergens may be more reactive to repeated accidental, diagnostic, or therapeutic challenge with such allergens. Such patients may be unresponsive to the usual doses of epinephrine used to treat anaphylactic reactions.

The preservative benzalkonium chloride may be absorbed by soft contact lenses. Patients who wear soft contact lenses should wait 5 minutes after instilling Betimol® before they insert their lenses.

Information for Patients
Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures.

Patients should also be instructed that ocular solutions can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions. (See PRECAUTIONS, General.)

Patients requiring concomitant topical ophthalmic medications should be instructed to administer these at least 5 minutes apart.

Patients with bronchial asthma, a history of bronchial asthma, severe chronic obstructive pulmonary disease, sinus bradycardia, second- or third-degree atrioventricular block, or cardiac failure should be advised not to take this product (See CONTRAINDICATIONS).

Drug Interactions
Beta-adrenergic blocking agents: Patients who are receiving a beta-adrenergic blocking agent orally and Betimol® should be observed for a potential additive effect either on the intraocular pressure or on the known systemic effects of beta-blockade.

Catecholamine-depleting drugs: Close observation of the patient is recommended when a beta-blocker is administered to patients receiving catecholamine-depleting drugs such as reserpine, because of possible additive effects and the production of hypotension and/or marked bradycardia, which may produce vertigo, syncope, or postural hypotension.

Calcium antagonists: Caution should be used in the co-administration of beta-adrenergic blocking agents and oral or intravenous calcium antagonists, because of possible atrioventricular conduction disturbances, left ventricular failure, and hypotension. In patients with impaired cardiac function, co-administration should be avoided.

Digitalis and calcium antagonists: The concomitant use of beta-adrenergic blocking agents with digitalis and calcium antagonists may have additive effects in prolonging atrioventricular conduction time.

Injectable Epinephrine: (See PRECAUTIONS, General, Anaphylaxis.)

Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenicity of timolol (as the maleate) has been studied in mice and rats. In a two-year study orally administered timolol maleate
DOSAGE AND ADMINISTRATION

Betimol® Ophthalmic Solution is available in concentrations of 0.25 and 0.5 percent. The usual starting dose is one drop of 0.25 percent Betimol® in the affected eye(s) twice a day. If the clinical response is not adequate, the dosage may be changed to one drop of 0.5 percent solution in the affected eye(s) twice a day.

If the intraocular pressure is maintained at satisfactory levels, the dosage schedule may be changed to one drop once a day in the affected eye(s). Since in some patients the pressure-lowering response to Betimol® may require a few weeks to stabilize, evaluation should include a determination of intraocular pressure after approximately 4 weeks of treatment with Betimol®.

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DOSAGES above one drop of 0.5 percent Betimol® twice a day generally have not been shown to produce further reduction in intraocular pressure. If the patient’s intraocular pressure is still not at a satisfactory level on this regimen, concomitant therapy with pilocarpine and other miotics, and/or epinephrine, and/or systemically administered carbonic anhydrase inhibitors, such as acetazolamide can be instituted.

OVERDOSAGE

No information is available on overdosage with Betimol®. Symptoms that might be expected with an overdose of a beta-adrenergic receptor blocking agent are bronchospasm, hypotension, bradycardia, and acute cardiac failure.

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HOW SUPPLIED

Betimol® (timolol ophthalmic solution) is a clear, colorless solution.

Betimol® 0.25% is supplied in a white, opaque, plastic, ophthalmic dispenser bottle with a controlled drop tip as follows:

- NDC 76478-001-05 5 mL fill in 5 cc container
- NDC 76478-001-10 10 mL fill in 11 cc container
- NDC 76478-001-15 15 mL fill in 15 cc container

Betimol® 0.5% is supplied in a white, opaque, plastic, ophthalmic dispenser bottle with a controlled drop tip as follows:

- NDC 76478-002-05 5 mL fill in 5 cc container
- NDC 76478-002-10 10 mL fill in 11 cc container
- NDC 76478-002-15 15 mL fill in 15 cc container

Rx Only

STORAGE

Store between 15° to 25°C (59° to 77°F). Do not freeze. Protect from light.
DISCLAIMER

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