**7.1 Oral Beta-Adrenergic Receptor Inhibitors**

**5.11 Atopy/Anaphylaxis**

**5.10 Angle-Closure Glaucoma**

**5.9 Choroidal Detachment**

**5.7 Cerebrovascular Insufficiency**

**2 DOSAGE AND ADMINISTRATION**

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**1 INDICATIONS AND USAGE**

**FULL PRESCRIBING INFORMATION: CONTENTS***

- **Contraindications**
- **Warnings**
- **Precautions**
- **Adverse Reactions**
- **Drug Interactions**

**7.1 Oral Beta-Adrenergic Receptor Inhibitors**

- **Blepharitis, conjunctivitis, crusting, ocular irritation; decreased visual acuity; diplopia; pseudopemphigoid; choroidal detachment**

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**WARNINGS AND PRECAUTIONS**

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**7.1 Oral Betadex Argent Receptor Inhibitors**

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**REFERENCES**

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**7.1 Oral Betadex Argent Receptor Inhibitors**

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**FULL PRESCRIBING INFORMATION: CONTENTS***

**1 INDICATIONS AND USAGE**

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**DOSAGE AND ADMINISTRATION**

**5.1 General**

- Beta-adrenergic receptor inhibitors have experienced these adverse reactions. Oral beta-adrenergic receptor inhibitors may be administered with caution in diabetics subject to drug-induced hyperglycemia.

**5.2 Cardiac Failure**

- Beta-adrenergic receptor inhibitors may mask signs and symptoms of hypoglycemia and should be administered with caution in diabetic patients subject to drug-induced hypoglycemia.

**5.3 Bronchospasmodic Pneumonia**

- Beta-adrenergic receptor inhibitors may mask signs and symptoms of myocardial infarction and should be administered with caution in patients with coronary artery disease subject to drug-induced hypoglycemia.

**5.4 Surgical Anesthesia**

- Beta-adrenergic receptor inhibitors may mask signs and symptoms of acute myocardial infarction, postoperative cardiovascular depression, and postoperative hypotension. Thrombolytic agents may exacerbate the rebound hypertension which can follow the withdrawal of clonidine.

**5.5 Diabetes Mellitus**

- Beta-adrenergic receptor inhibitors should be administered with caution in diabetics subject to drug-induced hyperglycemia.

**5.6 Thyrotoxicosis**

- Beta-adrenergic receptor inhibitors may mask signs and symptoms of acute hypoglycemia.

**5.7 Cerebrovascular Insufficiency**

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Timolol maleate possesses an asymmetric carbon tert(-)-1-β-adrenergic receptor inhibitor. Its chemical

**DESCRIPTION**

showed that timolol was readily dialyzed from the gel. Upon contact with the precorneal tear film, fermentation by bacterium benzododecinium bromide 0.012%. polysorbate-80, and purified water. Preservative: tromethamine, boric acid, mannitol, maleate). Inactive ingredients: xanthan gum, mg of timolol maleate). Each mL of Timolol GFS supplied as a sterile, isotonic, buffered, aqueous

**CLINICAL PHARMACOLOGY**

was consistent. The results from the clinical trials showed that timolol was readily dialyzed from the gel. Upon contact with the precorneal tear film, fermentation by bacterium benzododecinium bromide 0.012%. polysorbate-80, and purified water. Preservative: tromethamine, boric acid, mannitol, maleate). Inactive ingredients: xanthan gum, mg of timolol maleate). Each mL of Timolol GFS supplied as a sterile, isotonic, buffered, aqueous

**11. Replace screw cap by turning until firmly

**HOW TO USE THE DROP-TAINER® Bottle**

1. If you use other topically applied ophthalmic medications, they should be administered at least 10 minutes before Timolol GFS.
2. Wash hands before each use.
3. Before using the medication for the first time, be sure the Safety Seal on the bottle is unbroken.
4. Tear off the Safety Seal to break the seal.
5. Before each use, shake once and remove the screw cap.
6. Invert the bottle and hold the bottle between your thumb and middle finger, with the tips of the fingers pointing towards you.

**17. PATIENT COUNSELING INFORMATION**

7. Tilts your head back and position the bottle above the affected eye. DO NOT TOUCH THE EYE WITH THE TIP OF THE DROPER.
8. With the opposite hand, place a finger under the eye. Gently pull down until a “U” pocket is made between the lower lid and the eye.
9. With the hand holding the bottle, place your index finger on the bottom of the bottle. Push the bottom of the bottle to dispense the appropriate amount of medication. DO NOT SQUEEZE THE SIDES OF THE BOTTLE.
10. Repeat 6, 7, 8, and 9 with other eye if necessary.
11. Replace screw cap by turning firmly to ensure the bottle remains airtight.

**16. HOW SUPPLIED/STORAGE AND HANDLING**

Timolol GFS, 0.25% timolol equivalent and 0.5% timolol equivalent, are both supplied as either 2.5 mL or 5 mL solution in a 5 mL white polyethylene bottle with a natural polyethylene drop tip and a yellow polyethylene overcap. Tamper-evidence is provided with a shrink band around the closure and neck area of the DROP-TAINER® package.

• 0.25% mL, NDC 61314-224-25
• 0.5% 2.5 mL, NDC 61314-224-25
• 0.5% 2.5 mL, NDC 61314-225-25
• 0.5% 2.5 mL, NDC 61314-225-25

Storage and handling

Store at 2º to 25ºC (36º to 77ºF). Protect from light.

**SANDOZ**

Manufactured by Alcon Laboratories, Inc.
Fort Worth, Texas 76134 for Alcon Laboratories, Inc., Princeton, NJ 08540

**9007201-1011**

**0.5% timolol maleate solution to healthy volunteers, maximum plasma concentrations were generally below 5 ng/mL. Doses higher than one drop of 0.5% Timolol GFS once daily have not been studied.

Pharmacokinetic studies in humans using this gel forming solution formulation were not performed. However, systemic uptake from a gel matrix is expected to be less than from a non-gel forming solution based on studies using other gel forming solutions. The maximum plasma timolol concentration from one drop is not expected to exceed those of the 0.5% timolol maleate solution.

**13 NONCLINICAL TOXICOLOGY**

**13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

In a two-year study of timolol maleate administered orally to rats, there was a marginal statistically significant increase in the incidence of adenomatous polyps in female rats administered 300 mg/kg/day (approximately 42,000 times the systemic exposure using the maximum recommended human ophthalmic dose). Similar differences were not observed in rats administered oral doses equivalent to approximately 14,000 times the maximum recommended human ophthalmic dose. In a lifetime oral study in mice, there were statistically significant increases in the incidences of benign and malignant pulmonary tumors, benign uterine polyps, and mammary adenocarcinomas in female mice at 500 mg/kg/day (approximately 700,000 times the systemic exposure following the maximum recommended human ophthalmic dose), but not at 5 or 50 mg/kg/day. An increased incidence of mammary adenocarcinomas in rodents has been associated with administration of several other therapeutic agents that elevate serum prolactin, but no correlation between serum prolactin levels and mammary tumors has been established in humans. Furthermore, in adult human female subjects who received oral doses of up to 60 mg of timolol maleate (the maximum recommended human oral dosage), there were no clinically meaningful changes in serum prolactin.

Timolol maleate was a base and betal 11. Replace screw cap by turning until firmly

**How to Use The DROP-TAINER® Bottle**

The DROP-TAINER® bottle is designed to assure the delivery of a precise medication. Before using your DROP-TAINER® bottle, read the complete instructions carefully.

1. If you use other topically applied ophthalmic medications, they should be administered at least 10 minutes before Timolol GFS.
2. Wash hands before each use.
3. Before using the medication for the first time, be sure the Safety Seal on the bottle is unbroken.
4. Tear off the Safety Seal to break the seal.
5. Before each use, shake once and remove the screw cap.
6. Invert the bottle and hold the bottle between your thumb and middle finger, with the tips of the fingers pointing towards you.

**14. CLINICAL STUDIES**

In controlled, double-masked, multicenter clinical studies, Timolol GFS administered once daily was shown to be equally effective in lowering intraocular pressure as the equivalent concentration of TIMOPTIC administered twice daily. Timolol GFS once daily was shown to be equally effective in lowering intraocular pressure as the equivalent concentration of TIMOPTIC administered twice daily. The effect of timolol in lowering intraocular pressure was evident for 24 hours with a single dose of Timolol GFS. Repeated observations over a three-month period study indicate that the intraocular pressure-lowering effect of Timolol GFS was consistent. The results from the clinical trials are shown in the following figures.

**12. PHARMACODYNAMICS**

In some patients the intraocular pressure-lowering response to Timolol GFS may require a few weeks to stabilize, evaluation should include a determination of intraocular pressure after approximately 4 weeks of treatment with Timolol GFS. If the patient’s intraocular pressure is still not at a satisfactory level on this regimen, concomitant therapy can be considered.

**12.2 Pharmacodynamics**

Focusing topical ocular administration of timolol to humans, low concentrations of drug are found in plasma. After bilateral administration of a