

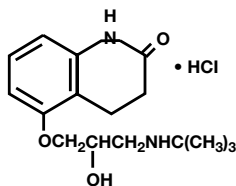
Carteolol Hydrochloride Ophthalmic Solution USP, 1%

Rx Only

Sterile

DESCRIPTION: Carteolol Hydrochloride Ophthalmic Solution USP, 1% is a nonselective beta-adrenoceptor blocking agent for ophthalmic use.

The chemical name for carteolol hydrochloride is (\pm) -5-[3-[(1,1-dimethylethyl) amino]-2-hydroxypropoxy]-3,4-dihydro-2(1H)-quinolinone monohydrochloride. The structural formula is as follows:



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$C_{16}H_{24}N_2O_3 \cdot HCl$

Mol. Wt. 328.84

Each mL of sterile solution contains **Active:** carteolol hydrochloride 10 mg (1%). **Preservative:** benzalkonium chloride 0.05 mg (0.005%). **Inactives:** sodium chloride, monobasic and dibasic sodium phosphate, sodium hydroxide and/or hydrochloric acid (to adjust pH to 6.0 - 8.0) and purified water.

CLINICAL PHARMACOLOGY:

Carteolol is a nonselective beta-adrenergic blocking agent with associated intrinsic sympathomimetic activity and without significant membrane-stabilizing activity.

Carteolol Hydrochloride reduces normal and elevated intraocular pressure (IOP) whether or not accompanied by glaucoma. The exact mechanism of the ocular hypotensive effect of beta-blockers has not been definitely demonstrated.

In general, beta-adrenergic blockers reduce cardiac output in patients in good and poor cardiovascular health. In patients with severe impairment of myocardial function, beta-blockers may inhibit the sympathetic stimulation necessary to maintain adequate cardiac function. Beta-adrenergic blockers may also increase airway resistance in the bronchi and bronchioles due to unopposed parasympathetic activity.

Given topically twice daily in controlled domestic clinical trials ranging from 1.5 to 3 months, Carteolol Hydrochloride produced a median percent reduction of IOP 22% to 25%. No significant effects were noted on corneal sensitivity, tear secretion, or pupil size.

INDICATIONS AND USAGE: Carteolol Hydrochloride Ophthalmic Solution 1% has been shown to be effective in lowering intraocular pressure and may be used in patients with chronic open-angle glaucoma and intraocular hypertension. It may be used alone or in combination with other intraocular pressure lowering medications.

CONTRAINDICATIONS: Carteolol is contraindicated in those individuals with bronchial asthma or with a history of bronchial asthma, or severe chronic obstructive pulmonary disease (see WARNINGS); sinus bradycardia; second- and third-degree atrioventricular block; overt cardiac failure (see WARNINGS); cardiogenic shock; or hypersensitivity to any component of this product.

WARNINGS: Carteolol has not been detected in plasma following ocular instillation. However, as with other topically applied ophthalmic preparations, Carteolol may be absorbed systemically. The same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. For example, severe respiratory reactions and cardiac reactions, including death due to bronchospasm in patients with asthma, and rarely death in association with cardiac failure, have been reported with topical application of beta-adrenergic blocking agents (see CONTRAINDICATIONS).

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 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. At the first sign or symptom of cardiac failure, Carteolol Hydrochloride should be discontinued.

Non-Allergic Bronchospasm: In patients with non-allergic bronchospasm or with a history of non-allergic bronchospasm (e.g., chronic bronchitis, emphysema), Carteolol Hydrochloride Ophthalmic Solution should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta₂ receptors.

Major Surgery: The necessity or desirability of withdrawal of beta-adrenergic blocking agents prior to 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. For these reasons, in patients undergoing elective surgery, gradual withdrawal of beta-adrenergic receptor blocking agents may be appropriate.

If necessary during surgery, the effects of beta-adrenergic blocking agents may be reversed by sufficient doses of such agonists as isoproterenol, dopamine, dobutamine or levarterenol (see OVERDOSAGE).

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:

General: Carteolol Hydrochloride Ophthalmic Solution should be used with caution in patients with known hypersensitivity to other beta-adrenoceptor blocking agents.

Use with caution in patients with known diminished pulmonary function.

In patients with angle-closure glaucoma, the immediate objective of treatment is to reopen the angle. This requires constricting the pupil with a miotic. Carteolol has little or no effect on the pupil. When Carteolol is used to reduce elevated intraocular pressure in angle-closure glaucoma, it should be used with a miotic and not alone.

Information to the Patient: For topical use only. To prevent contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use. Protect from light.

Risk from Anaphylactic Reaction: While taking beta-blockers, patients with a history of atopy or a history of severe anaphylactic reaction 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.

Muscle Weakness: Beta-adrenergic blockade has been reported to potentiate muscle weakness consistent with certain myasthenic symptoms (e.g., diplopia, ptosis and generalized weakness).

Drug Interactions: Carteolol Hydrochloride Ophthalmic Solution should be used with caution in patients who are receiving a beta-adrenergic blocking agent orally, because of the potential for additive effects on systemic beta-blockade.

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.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carteolol hydrochloride did not produce carcinogenic effects at doses up to 40 mg/kg/day in two-year oral rat and mouse studies. Test of mutagenicity, including the Ames Test, recombinant (rec)-assay, *in vivo* cytogenetics and dominant lethal assay demonstrated no evidence for mutagenic potential. Fertility of male and female rats and male and female mice was unaffected by administration of carteolol hydrochloride dosages up to 150 mg/kg/day.

Pregnancy: Teratogenic Effects: Pregnancy Category C: Carteolol hydrochloride increased resorptions and decreased fetal weights in rabbits and rats at maternally toxic doses approximately 1052 and 5264 times the maximum recommended human oral dose (10 mg/70 kg/day), respectively. A dose-related increase in wavy ribs was noted in the developing rat fetus when pregnant females received daily doses of approximately 212 times the maximum recommended human oral dose. No such effects were noted in pregnant mice subjected to up to 1052 times the maximum recommended human oral dose. There are no adequate and well-controlled studies in pregnant women. Carteolol Hydrochloride Ophthalmic Solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk, although in animal studies carteolol has been shown to be excreted in breast milk. Caution should be exercised when Carteolol Hydrochloride Ophthalmic Solution is administered to nursing mothers.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS: The following adverse reactions have been reported in clinical trials with Carteolol Hydrochloride Ophthalmic Solution.

Ocular: Transient eye irritation, burning, tearing, conjunctival hyperemia and edema occurred in about 1 of 4 patients. Ocular symptoms including blurred and cloudy vision, photophobia, decreased night vision, and ptosis and ocular signs including blepharconjunctivitis, abnormal corneal staining, and corneal sensitivity occurred occasionally.

Systemic: As is characteristic of nonselective adrenergic blocking agents, Carteolol may cause bradycardia and decreased blood pressure (See WARNINGS). The following systemic events have occasionally been reported with the use of Carteolol Hydrochloride Ophthalmic Solution: cardiac arrhythmia, heart palpitation, dyspnea, asthenia, headache, dizziness, insomnia, sinusitis, and taste perversion.

The following additional adverse reactions have been reported with ophthalmic use of beta₁ and beta₂ (nonselective) adrenergic receptor blocking agents:

Body As a Whole: Headache

Cardiovascular: Arrhythmia, syncope, heart block, cerebral vascular accident, cerebral ischemia, congestive heart failure, palpitation (see WARNINGS).

Digestive: Nausea

Psychiatric: Depression

Skin: Hypersensitivity, including localized and generalized rash

Respiratory: Bronchospasm (predominantly in patients with pre-existing bronchospastic disease), respiratory failure (see WARNINGS)

Endocrine: Masked symptoms of hypoglycemia in insulin-dependent diabetics (see WARNINGS)

Special Senses: Signs and symptoms of keratitis, blepharoptosis, visual disturbances including refractive changes (due to withdrawal of miotic therapy in some cases), diplopia, ptosis.

Other reactions associated with the oral use of nonselective adrenergic receptor blocking agents should be considered potential effects with ophthalmic use of these agents.

OVERDOSAGE: No specific information on emergency treatment of overdosage in humans is available. Should accidental ocular overdosage occur, flush eye(s) with water or normal saline. The most common effects expected with overdosage of a beta-adrenergic blocking agent are bradycardia, bronchospasm, congestive heart failure and hypotension.

In case of ingestion, treatment with Carteolol Hydrochloride Ophthalmic Solution should be discontinued and gastric lavage considered. The patient should be closely observed and vital signs carefully monitored. The prolonged effects of carteolol must be considered when determining the duration of corrective therapy. On the basis of the pharmacologic profile, the following additional measures should be considered as appropriate:

Symptomatic Sinus Bradycardia or Heart Block: Administer atropine. If there is no response to vagal blockade, administer isoproterenol cautiously.

Bronchospasm: Administer a beta₂-stimulating agent such as isoproterenol and/or a theophylline derivative.

Congestive Heart Failure: Administer diuretics and digitalis glycosides as necessary.

Hypotension: Administer vasopressors such as intravenous dopamine, epinephrine or norepinephrine bitartrate.

DOSAGE AND ADMINISTRATION: The usual dose is one drop of Carteolol Hydrochloride Ophthalmic Solution 1% in the affected eye(s) twice a day.

If the patient's IOP is not at a satisfactory level on this regimen, concomitant therapy with pilocarpine and other miotics, and/or epinephrine or dipivefrin, and/or systemically administered carbonic anhydrase inhibitors, such as acetazolamide, can be instituted.

HOW SUPPLIED: Carteolol Hydrochloride Ophthalmic Solution USP, 1% is supplied as a sterile ophthalmic solution in plastic dispenser bottles of 5 mL (NDC 61314-238-05), 10 mL (NDC 61314-238-10) and 15 mL (NDC 61314-238-15). Store at 15° to 25°C (59° to 77°F) (room temperature) and protect from light.

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