

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Teoptic 1% w/v Eye Drops, Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Carteolol hydrochloride 1% w/v

Excipients with known effect: Benzalkonium chloride 0.005%.

For the full list of excipients, see Section 6.1

3 PHARMACEUTICAL FORM

Eye drops solution.

A clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the reduction of intraocular pressure e.g. in ocular hypertension, chronic open angle glaucoma, some secondary glaucomas.

4.2 Posology and method of administration

Posology

Adults: Initially one drop of 1% eye drops instilled twice daily in each affected eye.

If the clinical response is not adequate the dosage may be altered to one drop of 2% eye drops twice daily in each affected eye.

Elderly population: There is no indication that dosage needs to be modified for the elderly.

Paediatric population: Safety and effectiveness of carteolol has not been established.

Method of administration

Ocular use.

When using nasolacrimal occlusion or closing the eyelids for 2 minutes, the systemic absorption is reduced. This may result in a decrease in systemic side effects and an increase in local activity.

The dispenser remains sterile until the original closure is broken. Patients must be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures as this may contaminate the solution.

If the patient's IOP is not at a satisfactory level with this regimen, concomitant treatment with other IOP lowering drugs may be considered.

If more than one medication needs to be instilled in the eye, an interval of at least 5 minutes between application of the different medicinal products must be allowed.

4.3 Contraindications

The carteolol eye drops are contraindicated in patients with:

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Reactive airway disease including bronchial asthma, bronchospasms, or a history of bronchial asthma, severe chronic obstructive pulmonary disease.
- Sinus bradycardia, sick sinus syndrome, sino-atrial block, second or third degree atrioventricular block not controlled with pace-maker. Overt cardiac failure, cardiogenic shock.

4.4 Special warnings and precautions for use

Like other topically applied ophthalmic agents carteolol is absorbed systemically. Due to beta-adrenergic component, carteolol, the same types of cardiovascular, pulmonary and other adverse reactions seen with systemic beta-adrenergic blocking agents may occur.

Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. To reduce the systemic absorption, see 4.2.

Cardiac disorders

Patients with cardiovascular diseases (e.g. coronary heart disease, Prinzmetal's angina and cardiac failure) and hypotension therapy with beta-blockers should be critically assessed and the therapy with other active substances should be considered.

Patients with cardiovascular diseases should be watched for signs of deterioration of these diseases and of adverse reactions.

Due to its negative effect on conduction time, beta-blockers should only be given with caution to patients with first degree heart block.

Vascular disorders

Patients with severe peripheral circulatory disturbance/disorders (i.e. severe forms of Raynaud's disease or Raynaud's syndrome), untreated phaeochromocytoma and hypotension should be treated with caution.

Respiratory disorders

Respiratory reactions, including death due to bronchospasm in patients with asthma have been reported following administration of some ophthalmic betablockers.

Teoptic should be used with caution, in patients with mild/moderate chronic obstructive pulmonary disease (COPD) and only if the potential benefit outweighs the potential risk.

Hypoglycemia/diabetes

Beta-blockers should be administered with caution in patients subject to spontaneous hypoglycaemia or to patients with labile diabetes, as betablockers may mask the signs and symptoms of acute hypoglycaemia.

Beta-blockers should be administered with caution in patients with diabetic ketoacidosis or metabolic acidosis.

Beta-blockers may also mask the signs of hyperthyroidism

Corneal diseases

Ophthalmic beta-blockers may induce dryness of eyes. Patients with corneal diseases should be treated with caution.

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 intraocular pressure in angle-closure glaucoma it must be used with a miotic and not alone.

Other beta-blocking agents

The effect on intra-ocular pressure or the known effects of systemic betablockade may be potentiated when carteolol is given to the patients already receiving a systemic beta-blocking agent.

The response of these patients should be closely observed. The use of two topical beta-adrenergic blocking agents is not recommended (see section 4.5).

Anaphylactic reactions

While taking beta-blockers, patients with history of atopy or a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge with such allergens and unresponsive to the usual dose of adrenaline used to treat anaphylactic reactions.

Choroidal detachment

Choroidal detachment has been reported with administration of aqueous suppressant therapy (e.g. timolol, acetazolamide) after filtration procedures.

Surgical anaesthesia

β -blocking ophthalmological preparations may block systemic β -agonist effects e.g. of adrenaline. The anaesthetist should be informed when the patient is receiving carteolol.

Severe prolonged hypotension has been observed in some patients after administration of systemic beta-blockers during anaesthesia.

Nervous system disorders

Patients with myasthenia gravis should be treated with caution. Betaadrenergic blockade may potentiate muscle weakness related to certain myasthenic symptoms, such as diplopia, ptosis and generalised weakness.

Contact lenses

The carteolol eye drops contain benzalkonium chloride as a preservative. Therefore, the medicament should not be used while wearing soft contact lenses. The lenses must be removed before application of the drops and not reinserted earlier than 15 minutes after use.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

There is a potential for additive effects resulting in hypotension and/or marked bradycardia when ophthalmic beta-blocker solution is administered concomitantly with oral calcium channel blockers, beta-adrenergic blocking agents, anti-arrhythmics (including amiodarone), digitalis glycosides, parasympathomimetics, guanethidine.

Mydriasis resulting from concomitant use of ophthalmic beta-blockers and adrenaline (epinephrine) has been reported occasionally.

If a supplementary ophthalmic medication is used, there must be an interval of at least five minutes between the administration of the two products.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data for the use of carteolol in pregnant women. Carteolol should not be used during pregnancy unless clearly necessary. To reduce the systemic absorption, see 4.2.

Fertility

Epidemiological studies have not revealed malformative effects but show a risk for intra uterine growth retardation when beta-blockers are administered by the oral route. In addition, signs and symptoms of betablockade (e.g. bradycardia, hypotension, respiratory distress and hypoglycaemia) have been observed in the neonate when beta-blockers have been administered until delivery. If Teoptic 1% w/v Eye Drops, Solution is administered until delivery, the neonate should be carefully monitored during the first days of life.

Breast-feeding

Beta-blockers are excreted in breast milk. However, at therapeutic doses of carteolol in eye drops it is not likely that sufficient amounts would be present in breast milk

to produce clinical symptoms of beta-blockade in the infant. To reduce the systemic absorption, see 4.2.

4.7 Effects on ability to drive and use machines

As with any other eye medication, should a patient experience any disturbance of vision, dizziness or syncope following instillation of carteolol eye drops, driving and the operation of machinery must be avoided until vision has returned to normal.

4.8 Undesirable effects

Like other topically applied ophthalmic drugs, carteolol is absorbed into the systemic circulation. This may cause similar undesirable effects as seen with systemic beta-blocking agents. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. Listed adverse reactions include reactions seen within the class of ophthalmic beta-blockers.

Immune system disorders: Systemic allergic reactions including angioedema, urticaria, localized and generalized rash, pruritus, anaphylactic reaction.

Metabolism and nutrition disorders: Hypoglycaemia.

Psychiatric disorders: Insomnia, depression, nightmares, memory loss.

Nervous system disorders: Syncope, cerebrovascular accident, cerebral ischemia, increases in signs and symptoms of myasthenia gravis, dizziness, malaise, paraesthesia, and headache.

Other: Discomfort, sinusitis.

Eye disorders: Signs and symptoms of ocular irritation (e.g. burning, stinging, itching, tearing, redness), sensation of foreign body, blepharitis, keratitis, sensitivity to light (photophobia), conjunctivitis, oedema, blurred vision and choroidal detachment following filtration surgery (see 4.4 Special warnings and precautions for use), decreased corneal sensitivity, dry eyes, corneal erosion, ptosis, conjunctival hyperaemia, diplopia.

Cardiac disorders : Bradycardia, chest pain, palpitations, oedema, arrhythmia, congestive heart failure, atrioventricular block, cardiac arrest, cardiac failure.

Vascular disorders : Hypotension, Raynaud's phenomenon, cold hands and feet.

Respiratory, thoracic, and mediastinal disorders : Bronchospasm (predominantly in patients with pre-existing bronchospastic disease), dyspnoea, cough.

Gastrointestinal disorders: Dysgeusia, nausea, dyspepsia, diarrhoea, dry mouth, abdominal pain, vomiting.

Skin and subcutaneous tissue disorders: Alopecia, psoriasiform rash or exacerbation

of psoriasis, skin rash.

Musculoskeletal and connective tissue disorders: Myalgia.

Reproductive system and breast disorders: Sexual dysfunction, decreased libido.

General disorders and administration site conditions: Asthenia/fatigue.

Cases of corneal calcification have been reported very rarely in association with the use of phosphate containing eye drops in some patients with significantly damaged corneas.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard

4.9 Overdose

No specific information on emergency treatment of overdose in humans is available. Should accidental ocular overdose occur, the eyes should be flushed with water or saline solution.

The most common signs and symptoms to be expected following overdose with a beta-adrenergic receptor blocking agent include dizziness, headache, shortness of breath, symptomatic bradycardia, hypotension, bronchospasm, and acute cardiac failure.

In case of overdose standard medical treatment can be administered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiglaucoma preparations and miotics, beta blocking agents. ATC code: S01ED05

Carteolol is a non-selective beta-adrenergic blocking agent with associated intrinsic sympathomimetic activity (ISA) and without significant membrane stabilizing activity. It has been shown that beta blocking agents with ISA affect cardiac output, heart rate at rest, peripheral vascular resistance and consequently peripheral circulation less than beta blocking agents without ISA.

Carteolol reduces normal and elevated intraocular pressure whether or not accompanied by glaucoma. The exact mechanism of the ocular hypotensive effect of beta-blockers has not been definitely demonstrated. However, it appears that ophthalmic beta-adrenergic blocking agents mainly act by reducing aqueous humor production.

Given topically twice daily in controlled clinical trials, carteolol eye drops effectively reduced IOP in patients with glaucoma or ocular hypertension. No significant effects were noted on corneal sensitivity in healthy subjects or tear secretion or pupil size.

Administration of carteolol to the eyes of animals and healthy individuals has shown that carteolol increases the iris tissue blood velocity in the treated eye of rabbits and may increase tissue blood flow in the human optic nerve head.

Whereas topical nonselective beta-adrenergic blockers decrease serum HDL and worsen the total cholesterol/HDL ratio, beta-blockers with intrinsic sympathomimetic activity appear to have a lesser effect.

5.2 Pharmacokinetic properties

Absorption

A single ocular instillation of ¹⁴C-labelled carteolol hydrochloride 2% solution into rabbit eyes demonstrated that carteolol penetrates the cornea quickly. The highest concentration levels were found in the cornea, iris, anterior sclera, ciliary body and conjunctiva 30 to 60 minutes after dosing but declined rapidly to 5 to 10% of the maximum level after 8 hours.

Biotransformation

CYP2D6 mediated 8-hydroxylation is the only cytochrome P450 catalyzed metabolic reaction of carteolol. Carteolol has neither stimulatory nor inhibitory effects on CYP1A2, 2C9, 2C19, 2E1, and 3A4 activities. 8-Hydroxycarteolol was estimated to be more potent than carteolol in lowering IOP both in rabbits and in monkey. No data is available on metabolism after ocular application of carteolol in humans.

Elimination

One drop of a 2% carteolol hydrochloride solution was instilled in each eye of healthy volunteers. Approximately 16% of the dose was excreted in the urine as unchanged compound during the first 24 hours after instillation. The urinary elimination half-life was about 5 hours. The plasma level of carteolol hydrochloride after topical administration in the eye was below the detection limit (5ng/mL).

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of acute and repeated dose toxicity, genotoxicity, carcinogenic potential, and toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride	0.005	%
sodium chloride	0.7	%
sodium phosphate dibasic	0.1	%
sodium phosphate monobasic	0.04	%
water for injection to	100	%

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened: 24 months
Opened: 28 days

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

1 X 5ml polyethylene dropper bottle
3 X 5ml polyethylene dropper bottle

Not all pack sizes may be marketed

6.6 Special precautions for disposal

No special requirements for disposal.

7 MARKETING AUTHORISATION HOLDER

Laboratories Thea
12 Rue Louis Blériot
63017 Clermont-Ferrand Cedex 2
France

8 MARKETING AUTHORISATION NUMBER(S)

PL 20162/0007

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25 October 1991

Date of latest renewal: 27 November 2003

10 DATE OF REVISION OF THE TEXT

18/12/2015