

IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0290/061/002

Case No: 2064903

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Alcon Laboratories (UK) Ltd

Pentagon Park, Boundary Way, Hemel Hempstead, Hertfordshire HP2 7UD, England

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Betoptic 0.25% w/v Eye Drops, Suspension

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **16/06/2009**.

Signed on behalf of the Irish Medicines Board this

A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Betoptic 0.25% w/v Eye Drops, Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Betaxolol 0.25% w/v (as hydrochloride).

Excipients: Benzalkonium Chloride 0.01% w/v

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Eye drops, suspension

White to off-white, sterile, multidose, preserved suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

BETOPTIC SUSPENSION is indicated for the reduction of elevated intra-ocular pressure in patients with ocular hypertension and chronic open-angle glaucoma.

4.2 Posology and method of administration

The recommended dose is one drop in the affected eye(s) twice daily. In some patients, the intraocular pressure lowering responses to BETOPTIC SUSPENSION may require a few weeks to stabilize. As with any new medication, careful monitoring of patients is advised.

If the intraocular pressure of the patient is not adequately controlled on this regimen, concomitant therapy with pilocarpine and other miotics and/or epinephrine and/or carbonic anhydrase inhibitors can be instituted.

Children

Betoptic Suspension is not recommended for use in children.

4.3 Contraindications

Hypersensitivity to any component of this medication or to beta-adrenoceptor blockers. BETOPTIC SUSPENSION is contraindicated in patients with sinus bradycardia, and uncorrected greater than a first degree atrioventricular block, cardiogenic shock, or patients with overt cardiac failure.

4.4 Special warnings and precautions for use

Ophthalmic betaxolol has been shown to have a minor effect on heart rate and blood pressure in clinical studies. Caution should be used in treating patients with a history of cardiac failure or heart block. Treatment with BETOPTIC SUSPENSION should be discontinued at the first signs of cardiac failure.

Diabetes Mellitus: Beta-adrenergic blocking agents should be administered with caution in patients subject to spontaneous hypoglycaemia 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 hypoglycaemia.

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.

Major Surgery: Consideration should be given to the gradual withdrawal of beta-adrenergic blocking agents prior to general anesthesia because of the reduced ability of the heart to respond to beta-adrenergically mediated sympathetic reflex stimuli.

Pulmonary: Although cardioselective beta-blockers have less effect on lung function than non-selective beta-blockers, caution should be exercised in the treatment of glaucoma patients with obstructive pulmonary disease. There have been reports of asthmatic attacks and pulmonary distress during Betoptic treatment in such patients. In individual cases, the risk to benefit for each patient should be considered. An increase in airway resistance can be relieved by inhaled beta₂-mimetics.

In controlled clinical studies, ophthalmic betaxolol has shown minimal effect on pulmonary and cardiovascular parameters.

Ocular: In patients with angle-closure glaucoma, the immediate treatment objective is to reopen the angle by constriction of the pupil with a miotic agent. Betaxolol has little or no effect on the pupil. When BETOPTIC SUSPENSION is used to reduce elevated intraocular pressure in angle-closure glaucoma, it should be used with a miotic and not alone.

There have been reports of dry eyes associated with the topical ocular use of beta-blocking agents. Caution should be exercised in the use of beta-blocking agents in patients with Sicca Syndrome or similar tear film abnormalities.

Caution should be used when prescribing for patients with decreased immunoresponsiveness.

Safety and effectiveness in children have not been established.

BETOPTIC SUSPENSION is preserved with benzalkonium chloride, which may cause eye irritation. It is also known to discolour soft contact lenses and should not be used while the patient is wearing soft contact lenses. Contact lens wearers must remove their lenses prior to instillation of BETOPTIC SUSPENSION and wait for 15 minutes after dosing before reinserting the contact lenses.

4.5 Interaction with other medicinal products and other forms of interaction

Patients who are receiving a beta-adrenergic blocking agent orally and BETOPTIC SUSPENSION should be observed for potential additive effect either on the intraocular pressure or on the known systemic effects of 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 bradycardia.

Betaxolol is an adrenergic blocking agent; therefore, caution should be exercised in patients using concomitant adrenergic psychotropic drugs.

Although a drug interaction is unlikely because of the low systemic levels attained with ophthalmic doses of betaxolol, caution should be exercised in patients who are receiving verapamil concurrently.

4.6 Pregnancy and lactation

Reproduction studies have been conducted with orally administered betaxolol HCl in rats and rabbits. There was evidence of drug related postimplantation loss in rabbits and rats at dose levels above 12 mg/kg and 128 mg/kg (1500 and 16,000 times the maximum recommended human ocular dose), respectively. Betaxolol HCl was not shown to be teratogenic, however, and there were no other adverse effects on reproduction at subtoxic dose levels. However, there are no adequate well controlled studies in pregnant women.

BETOPTIC SUSPENSION should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

It is not known whether betaxolol HCl is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when BETOPTIC SUSPENSION is administered to nursing women.

4.7 Effects on ability to drive and use machines

The ability to drive and use machines is unlikely to be affected following the use of BETOPTIC SUSPENSION.

4.8 Undesirable effects

Topically applied beta-adrenergic blocking agents may be absorbed systemically. Adverse reactions found with systemic administration of beta 1-adrenergic blocking agents may occur with topical administration (see 4.4 Special Warnings).

Ocular:

Transient ocular discomfort, such as ocular stinging and burning, blurred vision, corneal disease, such as corneal punctate staining, superficial punctate keratitis, foreign body sensation, photophobia, tearing, itching, erythema, may occur occasionally.

Allergic reactions, decreased corneal sensitivity, and dryness of eyes cannot be excluded.

Systemic:

Systemic reactions following topical administration of betaxolol have been rarely reported. These include:

Bradycardia, dyspnea, asthma, insomnia, headaches, depression, alopecia.

4.9 Overdose

No information is available on overdosage of humans after ocular application. The oral LD₅₀ of the drug ranged from 350-920 mg/kg in mice and 860-1050 mg/kg in rats. The symptoms which might be expected with an overdose of systemically administered beta-1-adrenergic receptor blocking agent are hypotension, bradycardia and acute cardiac failure.

No information is available on overdosage after ocular administration. A topical overdose of BETOPTIC SUSPENSION may be flushed from the eye(s) with warm tap water.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Betaxolol, a cardioselective (beta-1-adrenergic) receptor blocking agent, does not have significant membrane-stabilizing (local anaesthetic) activity and is devoid of intrinsic sympathomimetic action. Orally administered beta-adrenergic blocking agents may reduce cardiac output in healthy subjects and patients with heart disease. In patients with severe impairment of myocardial function, beta-adrenergic receptor antagonists may inhibit the sympathetic stimulatory effect necessary to maintain adequate cardiac function.

Betaxolol has no significant effect on pulmonary function as measured by Forced Expiratory Volume (FEV₁), Forced Vital Capacity (FVC), FEV₁/FVC and no evidence of cardiovascular beta-adrenergic-blockade during exercise was observed.

When instilled in the eye, betaxolol has the action of reducing elevated as well as normal intraocular pressure (IOP), whether or not accompanied by glaucoma. It is thought to produce this effect by reducing the rate of production of aqueous humour as demonstrated by tonography and aqueous fluorophotometry.

BETOPTIC SUSPENSION provides IOP lowering activity equivalent to that demonstrated by BETOPTIC Ophthalmic Solution 0.5%. Elevated IOP presents a major risk factor in glaucomatous field loss. The higher the level of IOP, the greater the likelihood of optic nerve damage and visual field loss. Ophthalmic betaxolol has little or no effect on the constriction of the pupil and minimal effect on pulmonary and cardiovascular function.

5.2 Pharmacokinetic properties

The onset of action of betaxolol can generally be noted within 30 minutes and the maximal effect can usually be detected 2 hours after topical administration. A single dose provides a 12-hour reduction in intraocular pressure.

The polar nature of betaxolol can produce apparent ocular discomfort. In this formulation, betaxolol molecules are ionically bound to the amberlite resin. Upon instillation the betaxolol molecules are displaced by ions in the tear film. This displacement process occurs over several minutes and enhances the ocular comfort observed for BETOPTIC Suspension.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
 Poly (styrene divinylbenzene) sulphonic acid
 Carbomer
 Mannitol
 N-Lauroylsarcosine
 Boric acid
 Disodium edetate
 Hydrochloric acid and/or sodium hydroxide (for pH adjustment)
 Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

Unopened: 2 years
 Once opened: Discard 4 weeks after first opening.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

BETOPTIC SUSPENSION is packaged as a 5 mL label fill in a 5 mL and a 10 mL label fill in a 10 mL natural low density polyethylene (LDPE), DROP-TAINER[®] with a LDPE dispensing plug and a 15 mm white polypropylene closure. The DROP-TAINER[®] utilizes a tamper evident closure with a break away ring.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Shake before each use.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Alcon Laboratories (UK) Ltd.
Pentagon Park
Boundary Way
Hemel Hempstead
Hertfordshire, HP2 7UD
England

8 MARKETING AUTHORISATION NUMBER

PA 290/61/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21 October 1993

Date of last renewal: 21 October 2008

10 DATE OF REVISION OF THE TEXT

January 2009