Betoptic 0.5% w/v Eye Drops Suspension

Summary of Product Characteristics Updated 04-Oct-2022 | Novartis

1. Name of the medicinal product

Betoptic 0.5% w/v eye drops, solution

2. Qualitative and quantitative composition

Betaxolol 0.5% w/v (as hydrochloride)

Excipients with known effect: 1ml of solution contains 0.1mg benzalkonium chloride.

For a full list of excipients see Section 6.1

3. Pharmaceutical form

Eye Drops, Solution

4. Clinical particulars

4.1 Therapeutic indications

Betoptic is indicated for the reduction of elevated intraocular pressure in patients with ocular hypertension and chronic open angle glaucoma.

4.2 Posology and method of administration

Adults (including the elderly)

The usual dose is one drop to be instilled into the affected eye(s) twice daily.

Children

Betoptic is not recommended for use in children.

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.

After cap is removed, if tamper evident snap collar is loose, remove before using product.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients.
- Reactive airway disease including severe bronchial asthma or a history of severe 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

For ocular use only.

General: Like other topically applied ophthalmic agents, betaxolol is absorbed systemically. Due to the beta-adrenergic component, betaxolol, the same types of cardiovascular, pulmonary and other adverse reactions seen with systemic betaadrenergic blocking agents may occur. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. To reduce the systemic absorption, see section 4.2.

Cardiac disorders: In patients with cardiovascular diseases (e.g. coronary heart disease, Prinzmetal's angina and cardiac failure) and hypotension, therapy with betablockers 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) 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 beta-blockers.

Patients with mild/moderate bronchial asthma, a history of mild/moderate bronchial asthma or, mild/moderate chronic obstructive pulmonary disease (COPD) should be treated with caution.

Hypoglycaemia/Diabetes: Beta-blockers should be administered with caution in patients subject to spontaneous hypoglycaemia or to patients with labile diabetes, as beta-blockers may mask the signs and symptoms of acute

hypoglycaemia. While Betoptic has demonstrated a low potential for systemic effects, it should be used with caution in patients suspected of developing thyrotoxicosis.

Hyperthyroidism: Beta-blockers may also mask the signs of hyperthyroidism.

Muscle weakness: Beta adrenergic blocking agents have been reported to potentiate muscle weakness consistent with certain myasthenic symptoms (e.g. diplopia, ptosis and generalised weakness).

Corneal diseases: In patients with angle-closure glaucoma, the immediate treatment objective is to re-open the angle by constriction of the pupil with a miotic agent, betaxolol has no effect on the pupil, therefore, Betoptic should be used with a miotic to reduce elevated intraocular pressure in angle-closure glaucoma.

Ophthalmic beta-blockers may induce dryness of eyes. Caution should be exercised in the use of beta-blocking agents in patients with corneal diseases, Sicca Syndrome or similar tear film abnormalities.

Other beta-blocking agents: The effect on intra-ocular pressure or the known effects of systemic beta-blockade may be potentiated when betaxolol 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 a 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: Beta-blocking ophthalmological preparations may block systemic beta-agonist effects e.g. of adrenaline. The anaesthesiologist should be informed when the patient is receiving betaxolol. Consideration should be given to the gradual withdrawal of beta-adrenergic blocking agents prior to general anaesthesia because of the reduced ability of the heart to respond to beta-adrenergically mediated sympathetic reflex stimuli.

Contact lenses: Betoptic Eye Drops contains 0.5 mg Benzalkonium Chloride in each 5 ml which is equivalent to 0.1 mg/ml. Benzalkonium chloride may be absorbed by soft contact lenses and may change the colour of the contact lenses. In case patients are allowed to wear contact lenses, they must be instructed to remove contact lenses prior to application of Betoptic eye drops, suspension and wait 15 minutes after instillation of the dose before reinsertion.

From the limited data available, there is no difference in the adverse event profile in children compared to adults. Generally, however, eyes in children show a stronger reaction for a given stimulus than the adult eye. Irritation may have an effect on treatment adherence in children Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. Should be used with caution in dry eye patients and in patients where the cornea may be compromised. Patients should be monitored in case of prolonged use.

4.5 Interaction with other medicinal products and other forms of interaction

No specific drug interaction studies have been performed with betaxolol.

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

Betablockers can decrease the response to adrenaline use to treat anaphylactic reactions. Special caution should be exercised in patients with a history of atophy or anaphylaxis.

Caution should be exercised in patients using concomitant adrenergic psychotropic drugs.

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

If more than one topical ophthalmic medicinal product is being used, the medicines must be administered at least 5 minutes apart. Eye ointments should be administered last

4.6 Fertility, pregnancy and lactation

Fertility

There are no data on the effects of Betaxolol Eye Drops on human fertility.

Pregnancy

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

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 beta-blockade (e.g. bradycardia, hypotension, respiratory distress and hypoglycaemia) have been observed in the neonate when beta-blockers have been administered until delivery. If BETOPTIC SOLUTION is administered until delivery, the neonate should be carefully monitored during the first days of life.

Lactation

Beta-blockers are excreted in breast milk, having the potential to cause serious undesirable effects in the infant of the nursing mother. However, at therapeutic doses of betaxolol in eye drops, it is not likely that sufficient amounts would be present in breast milk to produce clinical symptoms of betablockade in the infant. To reduce systemic absorption, see section 4.2.

4.7 Effects on ability to drive and use machines

Betoptic 0.5% eye drops, solution has no or negligible influence on the ability to drive and use machines

Temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs after instillation, the patient must wait until the vision clears before driving or using machinery.

4.8 Undesirable effects

Like other topically applied ophthalmic drugs, betaxolol is absorbed into the systemic circulation. This may cause similar undesirable effects as seen with systemic betablocking 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.

Summary of the safety profile

In clinical trials with Betaxolol eye drops the most common adverse reaction was ocular discomfort, occurring in 12.0% of patients.

The following adverse reactions have been reported during clinical trials or post marketing surveillance with Betaxolol eye drops and are classified according to the subsequent convention: very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and frequency unknown/cannot be estimated from the available data.

Within each frequency-grouping, adverse reactions are presented in order of decreasing seriousness.

System Organ Classification	MedDRA Preferred Term (V 13.0)
Inmmune system disorders	*Frequency unknown:* hypersensitivity

Psychiatric disorders	*Rare:* anxiety, insomnia, depression
Nervous system disorders	*Common:* headache *Rare:* syncope *Frequency unknown:* dizziness
Eye disorders	*Very common:* ocular discomfort *Common:* vision blurred, lacrimation increased *Uncommon:* punctate keratitis, keratitis, conjunctivitis, blepharitis, visual impairment, photophobia, eye pain, dry eye, asthenopia, blepharospasm, eye pruritus, eye discharge, eyelid margin crusting, eye inflammation, eye irritation, conjunctival disorder, conjunctival oedema, ocular hyperaemia *Rare:* Cataract, decreased corneal sensitivity, erythema of eyelid
Cardiac disorders	*Uncommon:* bradycardia, tachycardia *Frequency unknown:* arrhythmia
Vascular disorders	*Rare:* hypotension
Respiratory, thoracic and mediastinal disorders	*Uncommon:* asthma, dyspnoea, rhinitis, *Rare:* cough, rhinorrhea
Gastrointestinal disorders	*Uncommon:* nausea *Rare:* dysgeusia
Skin and subcutaneous tissue disorders	*Rare:* dermatitis, rash, alopecia
Reproductive system and breast disorders	*Rare:* libido decreased
General disorders and administration site conditions	*Frequency unknown:* asthenia

Description of selected adverse reactions

Additional adverse reactions have been seen with ophthalmic beta-blockers and may potentially occur with BETOPTIC SOLUTION:

System Organ Classification	MedDRA Preferred Term (V13.0)
Immune system disorders:	*Frequency unknown:* Systemic allergic reactions including angioedema, urticaria, localized and generalized rash, pruritus, anaphylactic reaction.
Metabolism and nutrition disorders:	*Frequency unknown:* Hypoglycaemia.
Psychiatric disorders:	*Frequency unknown:* nightmares, memory loss, hallucinations, psychoses, confusion.
Nervous system disorders:	*Frequency unknown:* cerebrovascular accident, cerebral ischemia, increases in signs and symptoms of myasthenia gravis, paraesthesia
Eye disorders:	*Frequency unknown:* choroidal detachment following filtration surgery (see 4.4 Special warnings and special precautions for use), corneal erosion, ptosis, diplopia.
Cardiac disorders:	*Frequency unknown:* Chest pain, palpitations, oedema, congestive heart failure, atrioventricular block, cardiac arrest, cardiac failure. A slowed AV-conduction or increase of an existing AV-block

Vascular disorders:	*Frequency unknown:* Raynaud's phenomenon, cold and cyanotic hands and feet, Increase of an existing intermittent claudication.
Respiratory, thoracic, and mediastinal disorders:	*Frequency unknown:* Bronchospasm (predominantly in patients with pre-existing bronchspastic disease)
Gastrointestinal disorders:	*Frequency unknown:* dyspepsia, diarrhoea, dry mouth, abdominal pain, vomiting.
Skin and subcutaneous tissue disorders:	*Frequency unknown:* Psoriasiform rash or exacerbation of psoriasis
Musculoskeletal and connective tissue disorders:	*Frequency unknown:* Myalgia.
Reproductive system and breast disorders:	*Frequency unknown:* Sexual dysfunction, impotence.
General disorders and administration site conditions:	*Frequency unknown:* fatigue.

An increase in Anti Nuclear Antibodies (ANA) has been seen; its clinical relevance is unclear.

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 at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

In case of accidental ingestion, symptoms of overdose from betablockade may include bradycardia, hypotension, cardiac failure and bronchospasm.

If overdose with Betaxolol Eye Drops occurs, treatment should be symptomatic and supportive.

A topical overdose of Betoptic may be flushed from the eye(s) with warm tap water.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Ophthalmologicals: Antiglaucoma Preparations & Miotics. ATC Code: SO1E D02

Betaxolol is a cardioselective Beta1 receptor blocker which, when applied topically to the eye, lowers intraocular pressure. It is thought to produce this effect by reducing the rate of production of aqueous humour.

Clinical Pharmacology

Several studies have indicated that betaxolol may have a beneficial effect on visual function for up to 48 months in patients with chronic open-angle glaucoma and up to 60 months in patients with ocular hypertension. Moreover there is evidence that betaxolol maintains or increases ocular blood flow/perfusion.

5.2 Pharmacokinetic properties

Betaxolol is highly lipophilic which results in good permeation of the cornea, allowing high intraocular levels of the drug. Betaxolol is characterised by its good oral absorption, low first pass loss and a relatively long half-life of approx 16-22 hours. The elimination of betaxolol is primarily by the renal rather than faecal route. The major metabolic pathways yield two carboxylic acid forms plus unchanged betaxolol in the urine (approx. 16% of the administered dose).

5.3 Preclinical safety data

There are no preclinical 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

Disodium edetate, sodium chloride, benzalkonium chloride, sodium hydroxide, hydrochloric acid, purified water.

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store between 8-30°C.

Keep in the outer carton in order to protect from light.

6.5 Nature and contents of container

5 ml & 10 ml LDPE bottles (10 ml present in 15 ml container) with natural LDPE plug and blue polystyrene or polypropylene cap.

6.6 Special precautions for disposal and other handling

Do not touch the top of the bottle to any surface as this may contaminate the contents.

7. Marketing authorisation holder

Novartis Pharma AG Basel, Switzerland

8. Marketing authorisation number(s)

9. Date of first authorisation/renewal of the authorisation

10. Date of revision of the text

12/07/2022