

Summary of Product Characteristics

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1. NAME OF THE MEDICINAL PRODUCT

IOBET Eye Drops (Betaxolol Eye Drops 0.5 % w/v).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Betaxolol 0.5 % w/v

(As Betaxolol Hydrochloride 0.56 % w/v)

Benzalkonium Chloride..... 0.01 % w/v

(As preservative)

Water for Injection q.s.

3. PHARMACEUTICAL FORM

Ophthalmic Solution.

Description

A clear Colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

IOBET Eye Drops is indicated for the reduction of elevated intraocular pressure (IOP) in patients with ocular hypertension and chronic open angle glaucoma.

4.2 Posology and Method of Administration

For ocular use only.

Adults (including the elderly)

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

Paediatric Population

IOBET Eye Drops is not recommended for use in children.

Method of Administration

To prevent contamination of the dropper tip and solution, care must be taken not to touch the eyelids, surrounding areas, or other surfaces with the dropper tip of the bottle. Keep the bottle tightly closed when not in use. Discard unused solution, if any, four weeks after first opening the bottle/container.

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.

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.

Or, as directed by the physician.

Use the solution with one month after opening the vial.

4.3 Contraindications

IOBET Eye Drops is contraindicated in the following:

- Hypersensitivity to the betaxolol hydrochloride or to any of the excipients listed in section 6.1.
- 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 Special 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 beta-adrenergic blocking agents may occur. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration.

Cardiac disorders: In 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) 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 betaxolol 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, IOBET Eye Drops 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.

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.

Benzalkonium chloride (BKC): IOBET Eye Drops contains 0.01% w/v benzalkonium chloride as a preservative. Benzalkonium chloride has been reported to cause eye irritation, symptoms of dry eyes and may affect the tear film and corneal surface. This product 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

Contact lenses: Benzalkonium chloride (used as preservative) 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 IOBET Eye Drops and wait 15 minutes after instillation of the dose before reinsertion of contact lenses.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

No specific drug interaction studies have been performed with betaxolol eye drops.

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.

Beta-blockers can decrease the response to adrenaline use to treat anaphylactic reactions. Special caution should be exercised in patients with a history of atopy 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.

4.6 Fertility, Pregnancy and Lactation

Pregnancy

There are no adequate data for the use of betaxolol in pregnant women. Betaxolol should not be used during pregnancy unless clearly necessary.

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 betaxolol eye drops 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, 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 beta-blockade in the infant.

Fertility

There are no data on the effects of IOBET 0.5% Eye Drops on human fertility.

4.7 Effects on Ability to Drive and Use Machines

IOBET Eye Drops 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 beta-blocking agents. Incidence of systemic adverse effects after topical ophthalmic administration is lower than that of systemic administration. Listed adverse reactions include reactions seen within the class of ophthalmic beta-blockers.

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

Clinical trials or post-marketing experience

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 ($\geq 1/10$), common ($\geq 1/100$ to $<1/10$), uncommon ($\geq 1/1,000$ to $<1/100$), rare ($\geq 1/10,000$ 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	Adverse Events Frequency
Immune system disorders	<i>Frequency unknown:</i> Hypersensitivity.
Psychiatric disorders	<i>Rare:</i> Anxiety, insomnia, depression.
Nervous system disorders	<i>Common:</i> Headache. <i>Rare:</i> Syncope. <i>Frequency unknown:</i> Dizziness.
Eye disorders	<i>Very common:</i> Ocular discomfort. <i>Common:</i> Vision blurred, lacrimation increased. <i>Uncommon:</i> 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. <i>Rare:</i> Cataract, decreased corneal sensitivity, erythema of eyelid.
Cardiac disorders	<i>Uncommon:</i> Bradycardia, tachycardia. <i>Frequency unknown:</i> Arrhythmia.
Vascular disorders	<i>Rare:</i> Hypotension.

Respiratory, thoracic and mediastinal disorders	<i>Uncommon:</i> Asthma, dyspnoea, rhinitis. <i>Rare:</i> Cough, rhinorrhea.
Gastrointestinal disorders	<i>Uncommon:</i> Nausea. <i>Rare:</i> Dysgeusia.
Skin and subcutaneous tissue disorders	<i>Rare:</i> Dermatitis, rash, alopecia.
Reproductive system and breast disorders	<i>Rare:</i> Libido decreased.
General disorders and administration site conditions	<i>Frequency unknown:</i> Asthenia.

Following additional adverse reactions have been seen with ophthalmic beta-blockers and may potentially occur with Betaxolol Eye Drops:

System Organ Classification	Adverse Events Frequency
Immune system disorders	<i>Frequency unknown:</i> Systemic allergic reactions including angioedema, urticaria, localized and generalized rash, pruritus, anaphylactic reaction.
Metabolism and nutrition disorders	<i>Frequency unknown:</i> Hypoglycaemia.
Psychiatric disorders	<i>Frequency unknown:</i> Nightmares, memory loss, hallucinations, psychoses, confusion.
Nervous system disorders	<i>Frequency unknown:</i> Cerebrovascular accident, cerebral ischemia, increases in signs and symptoms of myasthenia gravis, paraesthesia.
Eye disorders	<i>Frequency unknown:</i> Choroidal detachment following filtration surgery, corneal erosion, ptosis, diplopia.
Cardiac disorders	<i>Frequency unknown:</i> 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	<i>Frequency unknown:</i> Raynaud's phenomenon, cold and cyanotic hands and feet, increase of an existing intermittent claudication.
Respiratory, thoracic, and mediastinal disorders	<i>Frequency unknown:</i> Bronchospasm (predominantly in patients with pre-existing bronchospastic disease).
Gastrointestinal disorders	<i>Frequency unknown:</i> Dyspepsia, diarrhoea, dry mouth, abdominal pain, vomiting.
Skin and subcutaneous tissue disorders	<i>Frequency unknown:</i> Psoriasiform rash or exacerbation of psoriasis.
Musculoskeletal and connective	<i>Frequency unknown:</i> Myalgia.

tissue disorders	
Reproductive system and breast disorders	<i>Frequency unknown: Sexual dysfunction, impotence.</i>
General disorders and administration site conditions	<i>Frequency unknown: Fatigue.</i>

Laboratory test findings

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 national reporting system.

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4.9 Overdose

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

If overdose with Betaxolol Eye Drops occurs, treatment should be symptomatic and supportive. A topical overdose may be flushed from the eye(s) with warm tap water.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic Group: Ophthalmologicals - Antiglaucoma Preparations and Miotics.

ATC Code: SO1E D02.

Mechanism of Action

Betaxolol is a cardioselective β_1 receptor blocker which, when applied topically to the eye, lowers intraocular pressure (IOP). It is thought to produce this effect by reducing the rate of production of aqueous humour.

Pharmacodynamic Effects

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 approximately 16 to 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 (approximately 16% of the administered dose).

5.3 Preclinical Safety Data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Disodium Edetate, Sodium Chloride, Benzalkonium Chloride, Sodium Hydroxide, Hydrochloric Acid, Water for Injection

6.2 Incompatibilities

None known.

6.3 Shelf-life

24 months.

6.4 Special Precautions for Storage

Store at a temperature not exceeding 30°C. Protect from light.

Store out of reach and sight of children.

6.5 Nature and Contents of Container

5 ml solution filled in 5 ml labeled LDPE vial with HIPS spike cap packed in a carton along with pack insert.

6.6 Special precautions for Disposal and Other Handling

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

7. MARKETING AUTHORISATION HOLDER

Registered office:

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8. MARKETING AUTHORISATION NUMBER(S)

Certificate no; 06027/07557/REN/2020

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Jun 01, 2021

10. DATE OF REVISION OF THE TEXT

August 2023.

11. REFERENCE(S)

Summary of Product Characteristics (SmPC) of BETOPTIC (Betaxolol) 0.5% w/v Eye Drops (revised on 07/2022) by Immedica Pharma AB, Sweden. Available at: <https://www.medicines.org.uk/emc/product/14098/smpc>. Accessed on July 17, 2023.