1.3 Product Information

	1.3.1	**Summary of Product Characteristics (if not identical to package insert)** **a) Proprietary name of a medicine** Betaxolol Hydrochloride 0.5%w/v eye drops (Ivyxolol eye drops) **b) Approved generic name(s)** Betaxolol Hydrochloride **c) Qualitative and quantitative composition** **Qualitative Composition:** This product contains: Betaxolol Hydrochloride BP **Quantitative Composition:** Each 5 ml contains: Betaxolol 5mg/ml (as Betaxolol Hydrochloride 5.6mg/ml) **d) Dosage form** Eye drops **e) Clinical particulars** **i.Therapeutic indication(s)** Reduction of elevated intraocular pressure in conditions such as ocular hypertension and chronic open-angle glaucoma. **ii.Route of administration** For topical administration to the eye only **iii. Contra-indications** This is contraindicated in patients with: - Sinus bradycardia, sick sinus syndrome, sinoatrial block - Cardiogenic shock - Overt cardiac failure - Second or third degree atrioventricular block not controlled with a pace-maker - Hypersensitivity to the active substance or any of the excipients or other beta blocking agents - Reactive airway disease including severe bronchial asthma or a history of severe bronchial asthma, sever chronic obstructive pulmonary disease - **iv.Special warnings and precautions for use** For ocular use only. General Like other topically applied ophthalmic drugs, betaxolol is absorbed systemically. Due to 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 administration is lower than for systemic administration. To reduce the systemic absorption, use nasolacrimal occlusion or close the eyelids for 2minutes. Cardiac disorders In patients with cardiovascular diseases (e.g. coronary heart disease, Prinzimetal'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 beta-blockers. Patients with mild/moderate bronchial asthmas, 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 generalized 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, Betaxolol should be used with a miotic to reduce elevated intraocular pressure in angle closure glaucoma. Ophthalmic beta-blockers may induce dryness of eyes. Patients with corneal diseased, Sicca syndrome or similar tea film abnormalities should be treated with caution. Other Beta-blocking agents The effect on intra-ocular pressure or the known effects of systemic blockade may be potentiaed 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 history of atopy or a history of sever 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. Considereation 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
This formulation of Betaxolol 0.5% Eye drops contains 0.1mg/ml benzalkonium chloride as a preservative which may be deposited in soft contact lenses. Hence Betaxolol 0.5% Eye drops should not be used while wearing these lenses. The lenses should be removed before instillation of the drops and not reinserted earlier than 15min after used.
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.

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye of surrounding structures.

Patients should also be instructed that ocular solutions, if handles improperly can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using. Patients should also be advised that if they develop any intercurrent ocular condition (e.g trauma, ocular surgery or infection), they should immediately seek their physician's advice concerning the continued use of present multi-dose container.

There have been reports of bacterial keratitis associated with the use of topical ophthalmic products.

v.Interactions

No specific drug interaction studies have been performed on Betaxolol.
There is a potential for additive effects resulting in hypotension and/ot 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 anaphylactiv 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 medical product is being used, the medicines must be administered at least 5 minutes apart. Eye ointments should be administered last.

vi. Fertility, pregnancy and lactation

Fertility

There are no data on the effects of Betaxolol eye drops on 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.
Epidemiological studies have not revealed malformative effects but show a high 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 administers until delivery. If Betaxolol eye drops 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 nursing mother.

vii. Effects on the ability to drive and operate machinery

Betaxolol 0.55 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.

viii. 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 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 with 12.0% of patients.

The following undesirable effects have been observed and reported with the following frequencies:
Very common: may affect more than 1 in 10 people
Common: may affect up to 1 in 10 people
Uncommon: may affect up to 1 in 100 people
Rare: may affect up to 1 in 1000 people
Very rare: may affect up to 1 in 10000 people
Not Known: frequency unknown/cannot be estimated from the available data
Within frequency-grouping, adverse reactions are presented in order of decreasing seriousness.

System organ classification	MedDRA Preferred Term
Immune 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 pruritis, 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, dyspneoe, rhinitis Rare: cough, rhinorrhea
Gastrointestinal disorders	Uncommon: nausea Rare: cough, 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: asthma.

Description of Selected adverse reactions

Additional adverse reactions have been seen with ophthalmic beta-blockers and may potentially occur with Betaxolol eye drops solution.

System Organ Classification	MedDRA Preferred Term
Immune system disorders	Frequency unknown: Systemic allergic reactions including angioedema, urticarial, localized and generalized rash, pruritis, 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, 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 bronchospastic disease)
Gastrointestinal disorders	Frequency unknown: dyspepsia, diarrhea, 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 still unclear.

ix. Overdose

In case of accidental ingestion, symptoms of overdose from betablockage may include bradycardia, hypotension, cardiac failure and bronchospasm.
If overdose with Betaxolol eye drops occurs, treatment should be symptomatic and supportive.
A topical overdoes of Betaxolol eye drops may be flushed from the eye(s) with warm tap water.

f) Pharmacological properties

i. Pharmacodynamic properties

Pharmacotherapeutic group:
Ophthalmologicals: Antiglaucoma
Preparations Miotics
ATC code: S01ED02

Betaxolol is a cardioselective $Beta_1$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 48months in patients with chronic open-angle glaucoma and up to 6 months patients with ocular hypertension. Moreover there is evidence that betaxolol maintains or increases ocular blood flow/perfusion.

ii.Pharmacokinetic properties

Betaxolol is hughly lipophilic which results in good permeation of the cornea, allowing high intraocular levels of the drug. Betaxolol is characterized by its good oral absorption, low first pass loss and a relatively long half-life of approximately 16-22hrs. 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.

iii.Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in the Summary of Product Characteristics.

g) Pharmaceutical particulars

1. Shelf-life

Unopened shelf-life is 24 months.

Opened shelf-life 28 days, but the patient is advised to discard any remaining drops after the prescribed course of treatment.

2. Special precautions for storage

It is recommended that the product be stored below (25˚C). Protect from direct light. Keep the product out of sight and reach of children.

3. Nature and composition of containers

5ml low density polyethylene bottles with a polypropylene spiked cap.

The Primary Packaging Material is Borealis, Bormed LE6609-PH low density polyethylene. This does not contain any additives and complies with European Pharmacopoeia regulations for containers for parenteral solutions.

4. Restriction on sale / distribution

Prescription Only Medicine

h) Administrative data

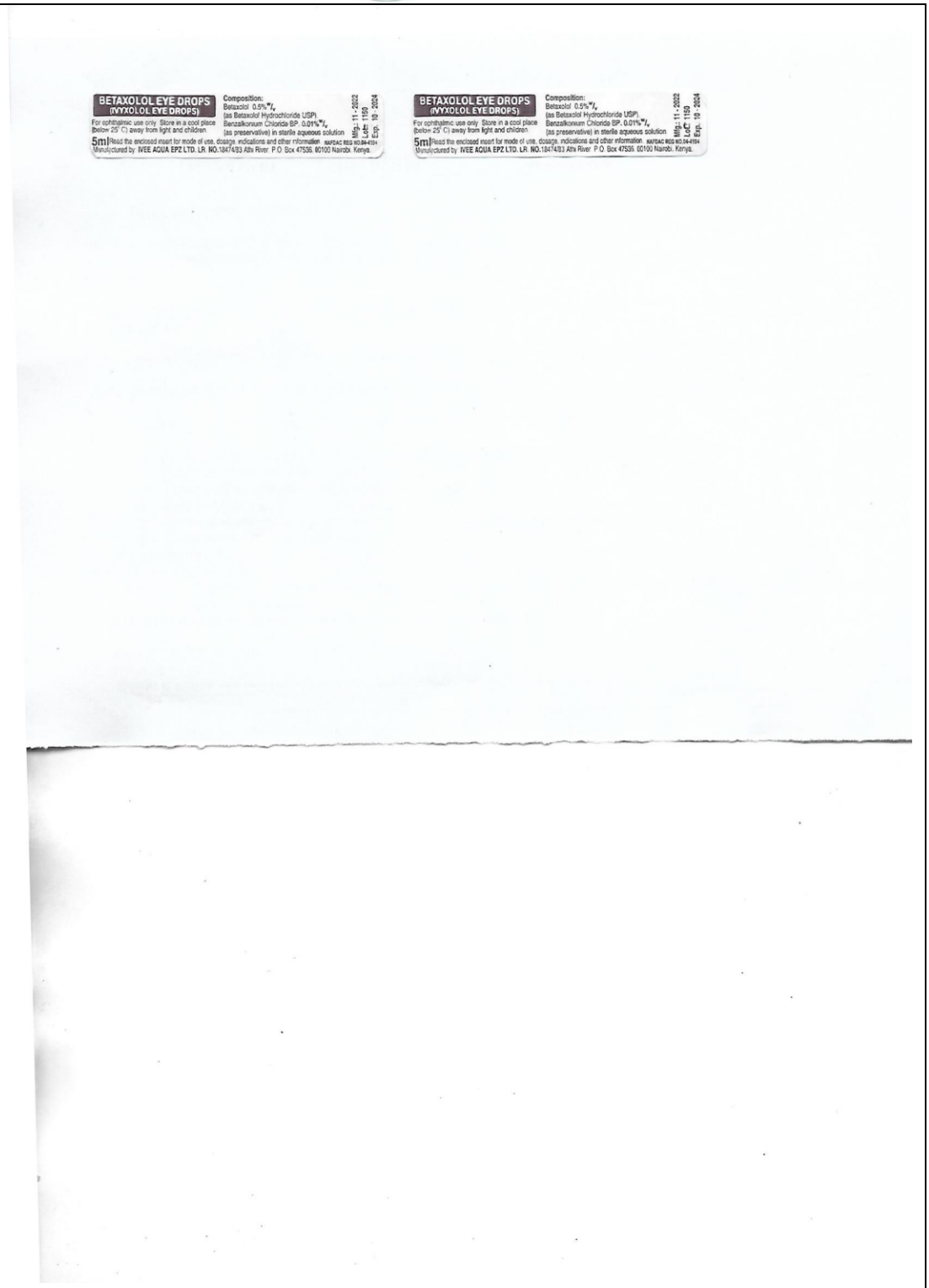
i. Name and address of holder of a registration. The name and address (business and postal) of the registration holder should be indicated

(Company) Name:	Ivee Aqua Epz Ltd.
Address:	P.O Box 25251, GPO 00100
	Nairobi, Kenya.
Country:	Kenya
Telephone:	+254-45-6622580
Telefax:	+254-45-6622581
e-mail:	**iveeaqua@ivee.co.ke**

ii. Date of first registration/renewal of a registration certificate. The date when the product was approved / when the registration was renewed should be indicated

Not applicable

	1.3.2	Labelling (outer & inner labels) 

		 BETAXOLOL EYE DROPS (IVYXOLOL EYE DROPS) Composition: Betaxolol 0.5%w/v (as Betaxolol Hydrochloride USP) Benzalkonium Chloride BP. 0.01%w/v (as preservative) in sterile aqueous solution For ophthalmic use only Store in a cool place (below 25° C) away from light and children 5ml Read the enclosed insert for mode of use, dosage, indications and other information NAFDAC REG NO.04-4194 Manufactured by IVEE AQUA EPZ LTD. LR. NO.18474/83 Athi River P.O. Box 47535. 00100 Nairobi. Kenya. Mfg.: 11 - 2022 Lot: 1159 Exp. 10 - 2024 BETAXOLOL EYE DROPS (IVYXOLOL EYE DROPS) Composition: Betaxolol 0.5%w/v (as Betaxolol Hydrochloride USP) Benzalkonium Chloride BP. 0.01%w/v (as preservative) in sterile aqueous solution For ophthalmic use only Store in a cool place (below 25° C) away from light and children 5ml Read the enclosed insert for mode of use, dosage, indications and other information NAFDAC REG NO.04-4194 Manufactured by IVEE AQUA EPZ LTD. LR. NO.18474/83 Athi River P.O. Box 47535. 00100 Nairobi. Kenya. Mfg.: 11 - 2022 Lot: 1159 Exp. 10 - 2024

	1.3.3	Package Insert (also known as patient information PIL)

IVYXOLOL EYE DROPS — **Patient Information Leaflet**

Please read this leaflet carefully before you start to use Ivyxolol Eye Drops.

What is in the bottle?

Ivyxolol Eye Drops contain the active ingredient Betaxolol Hydrochloride equivalent to 5 mg Betaxolol per ml. They also contain Benzalkonium Chloride, Sodium Phosphates, Disodium Edetate, Sodium Chloride and Water for Injection.

What are Ivyxolol Eye Drops used for?

Ivyxolol contains a substance called Betaxolol, which is a beta-blocker that is effective in reducing the pressure in your eye(s). You may be using Ivyxolol on its own or your doctor may have prescribed other medicine as well to treat the pressure in your eye(s). It is important that you continue to use **all** medicines prescribed by your doctor unless otherwise instructed by your doctor.

Before using Ivyxolol Eye Drops

In some circumstances this medicine may not be suitable for you and your doctor may wish to give you a different medicine, so:

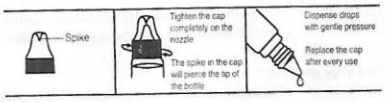
- If you have a history of heart failure, bradycardia (slow heart beat), heart block or other heart diseases
- If you are diabetic
- If you have an overactive thyroid gland
- If you have any form of lung disease or any condition that causes breathing difficulties e.g asthma
- If you are about to have an operation which requires a general anaesthetic
- If you are pregnant or intending to become pregnant
- If you are breast feeding a baby
- If you ever had to stop taking medicine because you were allergic to it

INFORM YOUR DOCTOR BEFORE STARTING TO USE THIS MEDICINE.

How to use Ivyxolol Eye Drops

- The normal dosage is one drop to be put in the affected eye twice a day. However, follow your doctor's advice.
- Do not touch the dropper tip to any surface as this may contaminate the solution.

Mode of use



While using Ivyxolol Eye Drops

Do not wear soft contact lenses whilst using Ivyxolol as the preservative may damage the lens.

What are the possible unwanted effects of Ivyxolol Eye Drops?

You may experience some or all of the following reactions in your eye:

- Discomfort, itching, foreign body gritty sensation, redness of the eye or inside the eyelid, staining or inflammation of the cornea, increased tear production, sensitivity to light, changes in pupil size and decreased sensitivity.
- You may also experience reactions in other parts of your body including sleeplessness, depression.
- If you experience any reactions listed or not listed above, after using Ivyxolol, then tell your doctor.

How to store Ivyxolol Eye Drops

- Store in a cool place (below 25°C) away from light.
- Discard any remaining solution one month after opening the bottle.
- Keep out of reach of children.

Who makes Ivyxolol Eye Drops?

Ivyxolol Eye Drops are made by **IVEE AQUA EPZ LTD**, L.R.18474/83, Athi River
P.O. Box No. 47536, 00100 Nairobi, Kenya

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