ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

IZBA 30 micrograms/mL eye drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One mL of solution contains 30 micrograms of travoprost.

Excipients with known effect

One mL of solution contains 7.5 mg propylene glycol and 2 mg polyoxyethylene hydrogenated castor oil 40 (HCO-40) (see section 4.4).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution (eye drops).

Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Decrease of elevated intraocular pressure in adult patients with ocular hypertension or open-angle glaucoma (see section 5.1).

Decrease of elevated intraocular pressure in paediatric patients aged 3 years to <18 years with ocular hypertension or paediatric glaucoma (see section 5.1).

4.2 Posology and method of administration

Posology

Use in adults, including elderly patients
The dose is one drop of travoprost in the conjunctival sac of the affected eye(s) once daily. Optimal effect is obtained if the dose is administered in the evening.

Nasolacrimal occlusion or gently closing the eyelid after administration is recommended. This may reduce the systemic absorption of medicinal products administered via the ocular route and result in a decrease in systemic adverse reactions.

If more than one topical ophthalmic medicinal product is being used, the medicinal products must be administered at least 5 minutes apart.

If a dose is missed, treatment should be continued with the next dose as planned. The dose should not exceed one drop in the affected eye(s) daily.

When substituting another ophthalmic antiglaucoma medicinal product with IZBA, the other medicinal product should be discontinued and IZBA should be started the following day.

Hepatic and renal impairment
Travoprost 30 µg/mL has not been studied in patients with hepatic or renal impairment. However, travoprost 40 µg/mL has been studied in patients with mild to severe hepatic impairment and in patients with mild to severe renal impairment (creatinine clearance as low as 14 mL/min). No dosage adjustment is necessary in these patients (see section 5.2). Therefore, no need for dose adjustment at the lower concentration of active ingredient is anticipated.

Paediatric population
IZBA can be used in paediatric patients from 3 years to <18 years at the same posology as in adults (see section 5.1).

The safety and efficacy of IZBA in children below the age of 3 years have not been established. Currently available data are described in section 5.1 but no recommendation on a posology below the age of 3 years can be made.

Method of administration

For ocular use.

For patients who wear contact lenses, please refer to section 4.4.

The patient should remove the protective overwrap immediately prior to initial use. 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.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Eye colour change

IZBA may gradually change the eye colour by increasing the number of melanosomes (pigment granules) in melanocytes. Before treatment is instituted, patients must be informed of the possibility of a permanent change in eye colour. Unilateral treatment can result in permanent heterochromia. The long-term effects on the melanocytes and any consequences thereof are currently unknown. The change in iris colour occurs slowly and may not be noticeable for months to years. The change in eye colour has predominantly been seen in patients with mixed coloured irides, i.e., blue-brown, grey-brown, yellow-brown and green-brown; however, it has also been observed in patients with brown eyes. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery in affected eyes, but the entire iris or parts of it may become more brownish. After discontinuation of therapy, no further increase in brown iris pigment has been observed.

Periorbital and eye lid changes

In controlled clinical trials, periorbital and/or eyelid skin darkening in association with the use of IZBA has been reported in 0.2% of patients.

Periorbital and lid changes including deepening of the eyelid sulcus have been observed with prostaglandin analogues.

IZBA may gradually change eyelashes in the treated eye(s); these changes were observed in about half of the patients in clinical trials and include: increased length, thickness, pigmentation, and/or number of lashes. The mechanism of eyelash changes and their long-term consequences are currently unknown.

There is no experience of IZBA in inflammatory ocular conditions; nor in neovascular, angle-closure, narrow-angle or congenital glaucoma and only limited experience in thyroid eye disease, in open-angle glaucoma of pseudophakic patients and in pigmentary or pseudoexfoliative glaucoma. IZBA should therefore be used with caution in patients with active intraocular inflammation.

Aphakic patients

Macular oedema has been reported during treatment with prostaglandin F2a analogues. Caution is recommended when using IZBA in aphakic patients, pseudophakic patients with a torn posterior lens capsule or anterior chamber lenses, or in patients with known risk factors for cystoid macular oedema.

Iritis/uveitis

In patients with known predisposing risk factors for iritis/uveitis, IZBA should be used with caution.

Contact with the skin

Skin contact with IZBA must be avoided as transdermal absorption of travoprost has been demonstrated in rabbits.

Prostaglandins and prostaglandin analogues are biologically active materials that may be absorbed through the skin. Women who are pregnant or attempting to become pregnant should exercise appropriate precautions to avoid direct exposure to the contents of the bottle. In the unlikely event of coming in contact with a substantial portion of the contents of the bottle, thoroughly cleanse the exposed area immediately.

Contact lenses

Patients must be instructed to remove contact lenses prior to application of IZBA and wait 15 minutes after instillation of the dose before reinsertion.

Excipients

IZBA contains propylene glycol which may cause skin irritation.
IZBA contains polyoxyethylene hydrogenated castor oil 40 which may cause skin reactions.

Paediatric population

No long-term safety data are available in the paediatric population.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/contraception

Travoprost must not be used in women of childbearing age/potential unless adequate contraceptive measures are in place (see section 5.3).

Pregnancy

Travoprost has harmful pharmacological effects on pregnancy and/or the foetus/new-born child. Travoprost should not be used during pregnancy unless clearly necessary.

Breast-feeding

It is unknown whether travoprost from eye drops is excreted in human breast milk. Animal studies have shown excretion of travoprost and metabolites in breast milk. The use of travoprost by breast-feeding mothers is not recommended.

Fertility

There are no data on the effects of travoprost on human fertility. Animal studies showed no effect of travoprost on fertility at doses more than 250 times the maximum recommended human ocular dose.

4.7 Effects on ability to drive and use machines

IZBA 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 at instillation, the patient must wait until the vision clears before driving or using machines.

4.8 Undesirable effects

Summary of the safety profile

In a clinical trial of 3 months duration (N=442) involving IZBA as monotherapy, the most common adverse reaction observed was hyperaemia of the eye (ocular or conjunctival) reported in approximately 12% of the patients.

Tabulated list of adverse reactions

The following adverse reactions were assessed to be related with IZBA monotherapy and are classified according to the following 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) and very rare (<1/10,000). Within each frequency grouping in Table 1, adverse reactions are presented in decreasing order of seriousness.

Table 1 Travoprost 30 µg/mL eye drops, solution

System Organ class	Frequency	Adverse reaction
Eye disorders	Very common	ocular hyperaemia
	Common	dry eye, eye pruritus, ocular discomfort
	Uncommon	punctate keratitis, anterior chamber inflammation, blepharitis, eye pain, photophobia, visual impairment, vision blurred, conjunctivitis, eyelid oedema, eyelid margin crusting, eye discharge, dark circles under eyes, growth of eyelashes, eyelash thickening
Skin and subcutaneous tissue disorders	Uncommon	pruritus, rash

The following adverse reactions were assessed to be related with travoprost 40 µg/mL eye drops, solution (either benzalkonium chloride [BAK] or Polyquad-preserved) and are classified according to the following 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 not known (cannot be estimated from the available data). Within each frequency grouping in Table 2, adverse reactions are presented in decreasing order of seriousness.

Table 2 Travoprost 40 µg/mL eye drops, solution

System Organ class	Frequency	Adverse reaction
Immune system disorders	Uncommon	hypersensitivity, seasonal allergy
Psychiatric disorders	Not known	depression, anxiety, insomnia
Nervous system disorders	Uncommon	headache
	Rare	dysgeusia, dizziness, visual field defect
Eye disorders	Very common	ocular hyperaemia
	Common	iris hyperpigmentation, eye pain, ocular discomfort, dry eye, eye pruritus, eye irritation
	Uncommon	corneal erosion, uveitis, iritis, anterior chamber inflammation, keratitis, punctate keratitis, photophobia, eye discharge, blepharitis, erythema of eyelid, periorbital oedema, eyelids pruritus, visual acuity reduced, vision blurred, lacrimation increased, conjunctivitis, ectropion, cataract, eyelid margin crusting, growth of eyelashes
	Rare	iridocyclitis, ophthalmic herpes simplex, eye inflammation, photopsia, eczema eyelids, conjunctival oedema, halo vision, conjunctival follicles, hypoaesthesia eye, trichiasis meibomianitis, anterior chamber pigmentation, mydriasis, asthenopia, eyelash hyperpigmentation, eyelash thickening
	Not known	macular oedema, lid sulcus deepened
Ear and labyrinth disorders	Not known	vertigo, tinnitus
Cardiac disorders	Uncommon	palpitations
	Rare	heart rate irregular, heart rate decreased
	Not known	chest pain, bradycardia, tachycardia, arrhythmia
Vascular disorders	Rare	blood pressure diastolic decreased, blood pressure systolic increased, hypotension, hypertension
Respiratory, thoracic and mediastinal disorders	Uncommon	cough, nasal congestion, throat irritation
	Rare	dyspnoea, asthma, respiratory disorder, oropharyngeal pain, dysphonia, rhinitis allergic, nasal dryness
	Not known	asthma aggravated, epistaxis
Gastrointestinal disorders	Rare	peptic ulcer reactivated, dry mouth gastrointestinal disorder, constipation
	Not known	diarrhoea, abdominal pain, nausea, vomiting
Skin and subcutaneous tissue disorders	Uncommon	skin hyperpigmentation (periocular), skin discolouration, hair texture abnormal, hypertrichosis
	Rare	dermatitis allergic, , dermatitis contact, erythema, rash, hair colour changes, madarosis
	Not known	Pruritus, hair growth abnormal
Musculoskeletal and connective tissue disorders	Rare	musculoskeletal pain, arthralgia
Renal and urinary disorders	Not known	dysuria, urinary incontinence
General disorders and administration site conditions	Rare	asthenia
Investigations	Not known	prostatic specific antigen increased

Paediatric population

In a 3-month phase 3 study and a 7-day pharmacokinetic study, involving 102 paediatric patients exposed to travoprost 40 micrograms/mL eye drops, solution, the types and characteristics of adverse reactions reported were similar to what has been observed in adult patients. The short-term safety profiles in the different paediatric subsets were also similar (see section 5.1). The most frequent adverse reactions reported in the paediatric population were ocular hyperaemia (16.9%) and growth of eyelashes (6.5%). In a similar 3-month study in adult patients, these events occurred at an incidence of 11.4% and 0%, respectively.

Additional adverse reactions reported in paediatric patients in the 3-month paediatric study (n=77) compared to a similar trial in adults (n=185) included erythema of eyelid, keratitis, lacrimation increased, and photophobia, all reported as single events with an incidence of 1.3% versus 0.0% seen in adults.

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 listed in Appendix V.

4.9 Overdose

A topical overdose is not likely to occur or to be associated with toxicity. A topical overdose of travoprost may be flushed from the eye(s) with lukewarm water. Treatment of a suspected oral ingestion is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Ophthalmologicals, antiglaucoma preparations and miotics, ATC code: S01EE04

Mechanism of action

Travoprost, a prostaglandin $F_{2\alpha}$ analogue, is a highly selective full agonist which has a high affinity for the prostaglandin FP receptor, and reduces the intraocular pressure by increasing the outflow of aqueous humour via trabecular meshwork and uveoscleral pathways. Reduction of the intraocular pressure in man starts about 2 hours after administration and maximum effect is reached after 12 hours. Significant lowering of intraocular pressure can be maintained for periods exceeding 24 hours with a single dose.

Clinical efficacy and safety

In a clinical trial, patients with open-angle glaucoma or ocular hypertension treated with IZBA dosed once-daily in the evening, demonstrated intraocular pressure lowering equivalent to travoprost 40 µg/mL eye drops, solution at all on-therapy visits and time points (95% CI within ±1.0 mmHg). The mean reduction from baseline in IOP ranged from 7.1 to 8.2 mmHg as summarised in Table 3. The mean percent reductions in IOP from baseline to each study visit and assessment time point ranged from 28.4% to 30.7%.

Table 3 IOP change from baseline (mmHg) for IZBA

Visit		8 AM	10 AM	4 PM
Week 2	Mean	-8.0	-7.3	-7.1
(N=442)	95% CI	(-8.3, -7.7)	(-7.6, -7.0)	(-7.4, -6.8)
Week 6	Mean	-8.1	-7.4	-7.2
(N=440*)	95% CI	(-8.4, -7.9)	(-7.6, -7.1)	(-7.5, -6.9)
Month 3	Mean	-8.2	-7.5	-7.1
(N=432*)	95% CI	(-8.6, -7.9)	(-7.9, -7.2)	(-7.4, -6.8)

*One subject had missing data at 8 AM at Week 6; one had missing data at 4 PM at Month 3.

An improved safety profile has been observed for IZBA when compared to the marketed travoprost 40 µg/mL eye drops, solution (benzalkonium chloride preserved or polyquaternium-1 perserved). The most common adverse reaction associated with both IZBA and travoprost 40 µg/mL eye drops, solution is hyperaemia. Hyperaemia (ocular or conjunctival) was observed in 11.8% of patients (N=442) exposed to IZBA compared with 14.5% observed for patients exposed to travoprost 40 µg/mL eye drops, solution, benzalkonium chloride preserved.

Secondary pharmacology

Travoprost significantly increased optic nerve head blood flow in rabbits following 7 days of topical ocular administration (1.4 micrograms, once-daily).

Travoprost 40 µg/mL eye drops, solution preserved with polyquaternium-1 induced minimal ocular surface toxicity, compared to eye drops preserved with benzalkonium chloride, on cultured human corneal cells and following topical ocular administration in rabbits.

Paediatric population

IZBA has not been specifically studied in a clinical trial involving paediatric subjects. However, a modelling approach demonstrated that IOP lowering would be expected to be equivalent in paediatric patients aged 3 years and above using both IZBA and TRAVATAN (travoprost 40 micrograms/mL eye drops, solution). The studies used in the model were two dose response trials, one Phase III study using IZBA and a paediatric study using TRAVATAN (travoprost 40 micrograms/mL eye drops, solution).

The efficacy of TRAVATAN (travoprost 40 micrograms/mL eye drops, solution) in paediatric patients from 2 months to less than 18 years of age was demonstrated in a 12-week, double-masked clinical study of travoprost compared with timolol in 152 patients diagnosed with ocular hypertension or paediatric glaucoma. Patients received either travoprost 0.004% once daily or timolol 0.5% (or 0.25% for subjects younger than 3 years old) twice daily. The primary efficacy endpoint was the intraocular pressure (IOP) change from baseline at Week 12 of the study. Mean IOP reductions in the travoprost and timolol groups were similar (see Table 4).

In the age groups 3 to <12 years (n=36) and 12 to <18 years (n=26), mean IOP reduction at Week 12 in the travoprost group was similar to that in the timolol group. Mean IOP reduction at Week 12 in the 2 months to <3 years of age group was 1.8 mmHg in the travoprost group and 7.3 mmHg in the timolol group. IOP reductions for this group were based on only 6 patients in the timolol group and 9 patients in the travoprost group where 4 patients in the travoprost group versus 0 patients in the timolol group had no relevant mean IOP reduction at Week 12. No data are available for children less than 2 months old.

The effect on IOP was seen after the second week of treatment and was consistently maintained throughout the 12 week period of study for all age groups.

Table 4 Comparison of Mean IOP Change from Baseline (mmHg) at Week 12

	Travoprost		Timolol			
	N	Mean (SE)	N	Mean (SE)	Mean Difference[a]	(95% CI)
	53	-6.4 (1.05)	60	-5.8 (0.96)	-0.5	(-2.1, 1.0)

SE = Standard Error; CI = Confidence Interval;
[a]Mean difference is travoprost – timolol. Estimates based on least squares means derived from a statistical model that accounts for correlated IOP measurements within patient where primary diagnosis and baseline IOP stratum are in the model.

5.2 Pharmacokinetic properties

Absorption

Travoprost is an ester prodrug. It is absorbed through the cornea where the isopropyl ester is hydrolysed to the active free acid. Studies in rabbits have shown peak concentrations of 20 ng/g of the free acid in aqueous humour one to two hours after topical dosing of travoprost 40 µg/mL eye drops, solution. Aqueous humour concentrations declined with a half-life of approximately 1.5 hours.

Distribution

Following topical ocular administration of travoprost 40 µg/mL eye drops, solution to healthy volunteers, low systemic exposure to active free acid was demonstrated. Peak active free acid plasma concentrations of 25 pg/mL or less were observed between 10 and 30 minutes post-dose. Thereafter, plasma levels declined rapidly to below the 10 pg/mL assay quantitation limit before 1 hour post-administration. Due to the low plasma concentrations and rapid elimination following topical dosing, the elimination half-life of active free acid in man could not be determined.

Biotransformation

Metabolism is the major route of elimination of both travoprost and the active free acid. The systemic metabolic pathways parallel those of endogenous prostaglandin $F_{2\alpha}$ which are characterised by reduction of the double bond in position C13-C14, oxidation of the 15-hydroxyl and β-oxidative cleavages of the upper side chain.

Elimination

Travoprost free acid and its metabolites are mainly excreted by the kidneys. Travoprost 40 µg/mL eye drops, solution has been studied in patients with mild to severe hepatic impairment and in patients with mild to severe renal impairment (creatinine clearance as low as 14 mL/min). No dosage adjustment is necessary in these patients.

Paediatric population

A pharmacokinetic study of TRAVATAN (travoprost 40 micrograms/mL eye drops, solution) in paediatric patients aged 2 months to <18 years demonstrated low plasma exposure to travoprost free acid, with concentrations ranging from below the 10 pg/mL assay limit of quantitation (BLQ) to 54.5 pg/mL.

5.3 Preclinical safety data

In ocular toxicity studies in monkeys, administration of travoprost at a dose of 0.45 microgram, twice a day, was shown to induce increased palpebral fissure. Topical ocular administration of travoprost to monkeys at concentrations of up to 0.012% to the right eye, twice daily for one year resulted in no systemic toxicity.

Increased palpebral fissure observed in monkeys were not seen in rabbits or in the clinical trials with travoprost products and is considered to be species specific.

Reproduction toxicity studies have been undertaken in rat, mice and rabbit by systemic route. Findings are related to FP receptor agonist activity in uterus with early embryolethality, post-implantation loss, foetotoxicity. In pregnant rat, systemic administration of travoprost at doses more than 200 times the clinical dose during the period of organogenesis resulted in an increased incidence of malformations. Low levels of radioactivity were measured in amniotic fluid and foetal tissues of pregnant rats administered ^{3}H-travoprost. Reproduction and development studies have demonstrated a potent effect on foetal loss with a high rate observed in rats and mice (180 pg/mL and 30 pg/mL plasma, respectively) at exposures 1.2 to 6 times the clinical exposure (up to 25 pg/mL).

Environmental risk assessment (ERA)

Travoprost is considered a persistent, bioaccumulative and toxic (PBT) substance. Hence, despite the very small amounts of travoprost used by patients in eye drops, a risk to the environment cannot be excluded.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polyquaternium-1
Polyoxyethylene hydrogenated castor oil 40 (HCO-40)
Boric acid (E284)
Mannitol (E421)
Sodium chloride
Propylene glycol (E1520)
Sodium hydroxide and/or hydrochloric acid (to adjust pH)
Purified water

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years.

Discard 4 weeks after first opening.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

IZBA is packaged in a 4 mL syndiotactic polypropylene (sPP) oval bottle with polypropylene (PP) dispensing plugs and closures presented in an overwrap. Each 4 mL bottle will contain 2.5 mL of solution.

Cartons containing 1 or 3 bottles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements. It should be noted that travoprost is considered a PBT substance (see section 5.3).

7. MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

8. MARKETING AUTHORISATION NUMBERS

EU/1/13/905/001-002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20 February 2014
Date of latest renewal: 14 November 2018

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

S.A. Alcon Couvreur N.V.
Rijksweg 14
B-2870 Puurs
Belgium

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON FOR SINGLE BOTTLE 4.0 mL + CARTON FOR 3 x 4.0 mL BOTTLES

1. NAME OF THE MEDICINAL PRODUCT

IZBA 30 micrograms/mL eye drops, solution
travoprost

2. STATEMENT OF ACTIVE SUBSTANCE

1 mL of solution contains 30 micrograms of travoprost

3. LIST OF EXCIPIENTS

Polyquaternium-1, polyoxyethylene hydrogenated castor oil 40 (HCO-40), boric acid, mannitol, sodium chloride, propylene glycol, sodium hydroxide and/or hydrochloric acid (to adjust pH) and purified water.

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Eye drops, solution

1 bottle of 2.5 mL
3 bottles of 2.5 mL

5. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.
Ocular use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP
Discard 4 weeks after first opening.
Opened:
Opened (1):
Opened (2)
Opened (3)

9. SPECIAL STORAGE CONDITIONS

10 SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBERS

EU/1/13/905/001 1 x 2.5 mL
EU/1/13/905/002 3 x 2.5 mL

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16 INFORMATION IN BRAILLE

IZBA

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

IZBA 30 micrograms/mL eye drops
travoprost
Ocular use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

2.5 mL

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

OVERWRAP

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

IZBA 30 micrograms/mL eye drops
travoprost
Ocular use

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.

3. EXPIRY DATE

EXP
Discard 4 weeks after first opening

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

2.5 mL

6. OTHER

B. PACKAGE LEAFLET

Package leaflet : Information for the user

IZBA 30 micrograms/mL eye drops, solution
travoprost

Read all of this leaflet carefully before you start using this medicine because it contains information important for you
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What IZBA is and what it is used for

IZBA **contains travoprost,** one of a group of medicines called **prostaglandin analogues**.
IZBA **is used to reduce high pressure in the eye in adults, adolescents and children from 3 years old onward.** This pressure can lead to an illness called **glaucoma.**

2. What you need to know before you use IZBA

Do not use IZBA
- **if you are allergic** to travoprost or any of the other ingredients of this medicine (listed in section 6).

Ask your doctor for advice if this applies to you.

Warnings and precautions

- IZBA **may increase** the length, thickness, colour and/or number of your **eyelashes.** Changes in the eyelids including unusual hair growth or in the tissues around the eye have also been observed.

- IZBA may gradually **change the colour of your iris** (the coloured part of your eye). This change may be permanent.

- If you have had cataract surgery talk to your doctor before you use IZBA. IZBA may increase the risk of inflammation of the back of the eye.

- If you have current or previous history of an eye inflammation (iritis and uveitis) talk to your doctor before you use IZBA. Eye inflammation is a possible side effect which may be associated with the use of prostaglandin analogues such as IZBA.

- **Travoprost** may be **absorbed through the skin. If any** of the medicinal product comes into **contact with the skin,** it should be **washed off** straight away. This is especially important in women who are pregnant or are attempting to become pregnant.

- If you wear soft contact lenses, do not use the drops with your lenses in. After using the drops wait 15 minutes before putting your lenses back in.

Talk to your doctor or pharmacist before using IZBA.

Children and adolescents
Use of IZBA is not recommended to those children under 3 years of age. The safety and efficacy of travoprost have not been established in this age group.

Other medicines and IZBA
Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Pregnancy and breast-feeding
Do not use IZBA if you are pregnant. The effects of this medicine in pregnant women are not known. If you think that you may be pregnant speak with your doctor right away. If you could become pregnant you must use adequate contraception whilst you use IZBA.

Do not use IZBA if you are breast-feeding. IZBA may get into your milk.

Driving and using machines
You may find that your vision is blurred for a time just after you use IZBA. Do not drive or use machines until this has worn off.

IZBA contains hydrogenated castor oil and propylene glycol which may cause skin reactions and irritation.

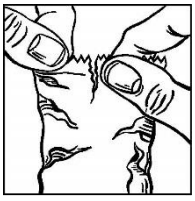
3. How to use IZBA

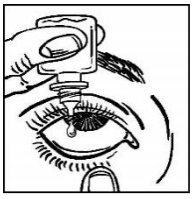
Always use this medicine exactly as your doctor or the doctor treating your child has told you. You should check with your doctor, the doctor treating your child or pharmacist if you are not sure.

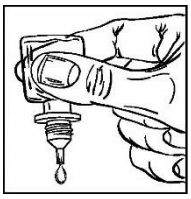
The recommended dose is

One drop in the affected eye or eyes, once a day in the evening.
Only use IZBA in both eyes if your doctor told you to. Use it for as long as your doctor or the doctor treating your child told you to.
IZBA can be used in children from 3 years to <18 years at the same dose as for adults.

IZBA should only be used as an eye drop.


1


2


3


4

- Immediately before using a bottle for the first time, tear open the overwrap pouch, take the bottle out (**picture 1**) and write the date of opening on the carton in the space provided.
- Wash your hands.
- Twist off the cap.
- Hold the bottle, pointing down, between your thumb and fingers.
- Tilt your head or your child's head gently back. Pull down the eyelid with a clean finger, until there is a 'pocket' between the eyelid and the eye. The drop will go in here (**picture 2**).
- Bring the bottle tip close to the eye. Use a mirror if it helps.
- **Do not touch the eye or eyelid, surrounding areas or other surfaces with the dropper.** It could infect the drops.
- Gently squeeze the bottle to release one drop of IZBA at a time. (**picture 3**).
- After using IZBA, keep the eyelid closed, apply gentle pressure by pressing a finger into the corner of the eye, by the nose (**picture 4**) for at least 1 minute. This helps to stop IZBA getting into the rest of the body.
- If you use drops in both eyes, repeat the steps for the other eye.
- Close the bottle cap firmly immediately after use.
- Only use one bottle at a time. Do not open the pouch until you need to use the bottle.

If a drop misses your eye, try again.

If you or your child are using other eye preparations such as eye drop or eye ointment, wait for at least 5 minutes between putting in IZBA and the other eye preparations.

If you or your child use more IZBA than you should
Rinse all the medicine out with warm water. Don't put in any more drops until it's time for your next regular dose. If IZBA is swallowed, consult your doctor or pharmacist immediately.

If you forget to use IZBA
Continue with the next dose as planned. Do not use a double dose to make up for a forgotten dose. Never use more than one drop in the affected eye(s) in a single day.

If you stop using IZBA
Do not stop using IZBA without first speaking to your doctor or the doctor treating your child, the pressure in your eye or your child's eye will not be controlled which could lead to loss of sight.

If you have any further questions on the use of this medicine, ask your doctor, the doctor treating your child or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects although not everybody gets them.

The following side effects have been observed with IZBA:

Very common: may affect more than 1 in 10 people

Effects in the eye: eye redness.

Common: may affect up to 1 in 10 people

Effects in the eye: eye discomfort, itchy eye, and dry eye.

Uncommon: may affect up to 1 in 100 people

Effects in the eye: inflammation inside the eye, eye surface inflammation with/out surface damage, inflammation of the eyelids, inflammation of the conjunctiva, eye pain, sensitivity to light, blurred or abnormal vision, swelling or crusting of eyelids, eye discharge, darkening of skin around the eye(s), growth and thickening of the eyelashes.

General side effects: rash or itching of the skin.

In addition, the following side effects have been observed with another medicine containing a higher strength of travoprost (40 micrograms/mL):

Very common: may affect more than 1 in 10 people

Effects in the eye: eye redness.

Common: may affect up to 1 in 10 people

Effects in the eye: changes in the colour of the iris (coloured part of the eye), eye irritation. eye pain, eye discomfort, dry eye, itchy eye.

Uncommon: may affect up to 1 in 100 people

Effects in the eye: corneal disorder, eye inflammation, iris inflammation, inflammation inside the eye, eye surface inflammation with/out surface damage, sensitivity to light, eye discharge, eyelid inflammation, eyelid redness, swelling around the eye, eyelid itching, blurred vision, increased tear production, infection or inflammation of the conjunctiva (conjunctivitis), abnormal turning outward of the lower eyelid, clouding of the eye, eyelid crusting, growth of eyelashes.

General side effects: increased allergic symptoms, headache, irregular heart beat, cough, stuffy nose, throat irritation, darkening of skin around the eye (s), skin darkening, abnormal hair texture, excessive hair growth.

Rare: may affect up to 1 in 1,000 people

Effects in the eye: perception of flashing lights, eczema of the eyelids, abnormally positioned eyelashes that grow back toward the eye, eye swelling, reduced vision, halo vision, decreased eye sensation, inflammation of the glands of the eyelids, pigmentation inside the eye, increase in pupil size, eyelash thickening, change in eyelash colour, tired eyes.

General side effects: eye viral infection, dizziness, bad taste, irregular or decreased heart rate, increased or decreased blood pressure, shortness of breath, asthma, nasal allergy or inflammation, nasal dryness, voice changes, gastrointestinal discomfort or ulcer, constipation, dry mouth, redness or itching of the skin, rash, hair colour change, loss of eyelashes, joint pain, musculoskeletal pain, generalised weakness.

Not known: frequency cannot be estimated from the available data

Effects in the eye: inflammation of the back of the eye, eyes appear more inset.

General side effects: depression, anxiety, insomnia, sensation of false movement, ringing in ears, chest pain, abnormal heart rhythm, increased heart beat, worsening of asthma, diarrhoea, nose bleeds, abdominal pain, nausea, vomiting, itching, abnormal hair growth, painful or involuntary urination, increase in prostate cancer marker.

In children and adolescents, the most common side effects seen with the medicine containing a higher strength of travoprost (40 micrograms/mL) are eye redness and growth of eyelashes. Both side effects were observed with a higher incidence in children and adolescents compared to adults.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store IZBA

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the bottle and the box after ‘EXP’. The expiry date refers to the last day of the month.

This medicine does not require any special storage conditions.

You must throw away the bottle 4 weeks after you first opened it, to prevent infections, and use a new bottle. Write down the date you opened it in the space on each carton box.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer used. These measures will help protect the environment.

6. Contents of the pack and other information

What IZBA contains
- The active substance is travoprost. Each mL of solution contains 30 micrograms of travoprost.
- The other ingredients are: polyquaternium-1, polyoxyethylene hydrogenated castor oil 40, propylene glycol (see end of section 2), sodium chloride, boric acid, mannitol and purified water. Tiny amounts of hydrochloric acid or sodium hydroxide are added to keep acidity levels (pH levels) normal.

What IZBA looks like and contents of the pack
IZBA eye drop is a liquid (a clear, colourless solution) supplied in a 4 mL plastic bottle with a screw cap. Each bottle contains 2.5 mL of travoprost eye drops and each bottle is placed in a pouch.

Pack sizes: 1 or 3 bottles.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

Manufacturer
S.A. Alcon Couvreur N.V.
Rijksweg 14
B-2870 Puurs
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Novartis Pharma N.V.
Tél/Tel: +32 2 246 16 11

България
Novartis Bulgaria EOOD
Тел.: +359 2 489 98 28

Česká republika
Novartis s.r.o.
Tel: +420 225 775 111

Danmark
Novartis Healthcare A/S
Tlf: +45 39 16 84 00

Deutschland
Novartis Pharma GmbH
Tel: +49 911 273 0

Eesti
SIA Novartis Baltics Eesti filiaal
Tel: +372 66 30 810

Lietuva
SIA Novartis Baltics Lietuvos filialas
Tel: +370 5 269 16 50

Luxembourg/Luxemburg
Novartis Pharma N.V.
Tél/Tel: +32 2 246 16 11

Magyarország
Novartis Hungária Kft.
Tel.: +36 1 457 65 00

Malta
Novartis Pharma Services Inc.
Tel: +356 2122 2872

Nederland
Novartis Pharma B.V.
Tel: +31 88 04 52 111

Norge
Novartis Norge AS
Tlf: +47 23 05 20 00

Ελλάδα
Novartis (Hellas) A.E.B.E.
Τηλ: +30 210 281 17 12

España
Novartis Farmacéutica, S.A.
Tel: +34 93 306 42 00

France
Novartis Pharma S.A.S.
Tél: +33 1 55 47 66 00

Hrvatska
Novartis Hrvatska d.o.o.
Tel. +385 1 6274 220

Ireland
Novartis Ireland Limited
Tel: +353 1 260 12 55

Ísland
Vistor hf.
Sími: +354 535 7000

Italia
Novartis Farma S.p.A.
Tel: +39 02 96 54 1

Κύπρος
Novartis Pharma Services Inc.
Τηλ: +357 22 690 690

Latvija
SIA Novartis Baltics
Tel: +371 67 887 070

Österreich
Novartis Pharma GmbH
Tel: +43 1 86 6570

Polska
Novartis Poland Sp. z o.o.
Tel.: +48 22 375 4888

Portugal
Novartis Farma - Produtos Farmacêuticos, S.A.
Tel: +351 21 000 8600

România
Novartis Pharma Services Romania SRL
Tel: +40 21 31299 01

Slovenija
Novartis Pharma Services Inc.
Tel: +386 1 300 75 50

Slovenská republika
Novartis Slovakia s.r.o.
Tel: + 421 2 5542 5439

Suomi/Finland
Novartis Finland Oy
Puh/Tel: +358 (0)10 6133 200

Sverige
Novartis Sverige AB
Tel: +46 8 732 32 00

United Kingdom (Northern Ireland)
Novartis Ireland Limited
Tel: +44 1276 698370

This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.