ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

AZOPT 10 mg/ml eye drops, suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of suspension contains 10 mg brinzolamide.

Excipient with known effect

Each ml of suspension contains 0.1 mg benzalkonium chloride.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, suspension.

White to off-white suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AZOPT is indicated to decrease elevated intraocular pressure in:
- ocular hypertension
- open-angle glaucoma

as monotherapy in adult patients unresponsive to beta-blockers or in adult patients in whom beta-blockers are contraindicated, or as adjunctive therapy to beta-blockers or prostaglandin analogues (see also section 5.1).

4.2 Posology and method of administration

Posology

When used as monotherapy or adjunctive therapy, the dose is one drop of AZOPT in the conjunctival sac of the affected eye(s) twice daily. Some patients may have a better response with one drop three times a day.

Special populations
Elderly population
No dose adjustment in elderly patients is necessary.

Hepatic and renal impairment
AZOPT has not been studied in patients with hepatic impairment and is therefore not recommended in such patients.

AZOPT has not been studied in patients with severe renal impairment (creatinine clearance < 30 ml/min) or in patients with hyperchloraemic acidosis. Since brinzolamide and its main metabolite are excreted predominantly by the kidney, AZOPT is therefore contra-indicated in such patients (see also section 4.3).

Paediatric population
The safety and efficacy of AZOPT in infants, children and adolescents aged 0 to 17 years have not been established. Currently available data are described in sections 4.8 and 5.1. AZOPT is not recommended for use in infants, children and adolescents.

Method of administration

For ocular use.

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

Instruct the patient to shake the bottle well before use. After the cap is removed, if tamper evident snap collar is loose, remove before using the product.

To prevent contamination of the dropper tip and suspension, care must be taken not to touch the eyelids, surrounding areas or other surfaces with the dropper tip of the bottle. Instruct patients to keep the bottle tightly closed when not in use.

When substituting another ophthalmic antiglaucoma agent with AZOPT, discontinue the other agent and start the following day with AZOPT.

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.

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) three times daily.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Known hypersensitivity to sulphonamides (see also section 4.4).
- Severe renal impairment.
- Hyperchloraemic acidosis.

4.4 Special warnings and precautions for use

Systemic effects

AZOPT is a sulphonamide inhibitor of carbonic anhydrase and, although administered topically, is absorbed systemically. The same types of adverse drug reactions that are attributable to sulphonamides may occur with topical administration, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). At the time of prescription, patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs of serious reactions or hypersensitivity occur, AZOPT should be withdrawn immediately.

Acid-base disturbances have been reported with oral carbonic anhydrase inhibitors. Use with caution in patients with risk of renal impairment because the possible risk of metabolic acidosis (see section 4.2).

Brinzolamide has not been studied in pre-term infants (less than 36 weeks gestational age) or those less than 1 week of age. Patients with significant renal tubular immaturity or abnormalities should only receive brinzolamide after careful consideration of the risk benefit balance because of the possible risk of metabolic acidosis.

Oral carbonic anhydrase inhibitors may impair the ability to perform tasks requiring mental alertness and/or physical coordination. AZOPT is absorbed systemically and therefore this may occur with topical administration.

Concomitant therapy

There is a potential for an additive effect on the known systemic effects of carbonic anhydrase inhibition in patients receiving an oral carbonic anhydrase inhibitor and AZOPT. The concomitant administration of AZOPT and oral carbonic anhydrase inhibitors has not been studied and is not recommended (see also section 4.5).

AZOPT was primarily evaluated in concomitant administration with timolol during adjunctive glaucoma therapy. Additionally the IOP-reducing effect of AZOPT as adjunctive therapy to the prostaglandin analogue travoprost has been studied. No long term data are available on the use of AZOPT as adjunctive therapy to travoprost(see also section 5.1).

There is limited experience with AZOPT in the treatment of patients with pseudoexfoliative glaucoma or pigmentary glaucoma. Caution should be used in treating these patients and close monitoring of intraocular pressure (IOP) is recommended. AZOPT has not been studied in patients with narrow-angle glaucoma and its use is not recommended in these patients.

The possible role of brinzolamide on corneal endothelial function has not been investigated in patients with compromised corneas (particularly in patients with low endothelial cell count). Specifically, patients wearing contact lenses have not been studied and careful monitoring of these patients when using brinzolamide is recommended, since carbonic anhydrase inhibitors may affect corneal hydration and wearing contact lenses might increase the risk for the cornea. Careful monitoring of patients with compromised corneas such as patients with diabetes mellitus or corneal dystrophies is recommended.

Benzalkonium chloride, which is commonly used as a preservative in ophthalmic products, has been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. Since AZOPT contains benzalkonium chloride, close monitoring is required with frequent or prolonged use in dry eye patients, or in conditions where the cornea is compromised.

AZOPT has not been studied in patients wearing contact lenses. AZOPT contains benzalkonium chloride which may cause eye irritation and is known to discolour soft contact lenses. Contact with soft contact lenses is to be avoided. Patients must be instructed to remove contact lenses prior to the application of AZOPT and wait at least 15 minutes after instillation of the dose before reinsertion.

Potential rebound effects following cessation of treatment with AZOPT have not been studied; the IOP-lowering effect is expected to last for 5-7 days.

Paediatric population

The safety and efficacy of AZOPT in infants, children and adolescents aged 0 to 17 years have not been established and its use is not recommended in infants, children or adolescents

4.5 Interaction with other medicinal products and other forms of interaction

Specific interaction studies with other medicinal products have not been performed with AZOPT.

In clinical studies, AZOPT was used concomitantly with prostaglandin analogues and timolol ophthalmic preparations without evidence of adverse interactions. Association between AZOPT and miotics or adrenergic agonists has not been evaluated during adjunctive glaucoma therapy.

AZOPT is a carbonic anhydrase inhibitor and, although administered topically, is absorbed systemically. Acid-base disturbances have been reported with oral carbonic anhydrase inhibitors. The potential for interactions must be considered in patients receiving AZOPT.

The cytochrome P-450 isozymes responsible for metabolism of brinzolamide include CYP3A4 (main), CYP2A6, CYP2C8 and CYP2C9. It is expected that inhibitors of CYP3A4 such as ketoconazole, itraconazole, clotrimazole, ritonavir and troleandomycin will inhibit the metabolism of brinzolamide by CYP3A4. Caution is advised if CYP3A4 inhibitors are given concomitantly. However, accumulation of brinzolamide is unlikely as renal elimination is the major route. Brinzolamide is not an inhibitor of cytochrome P-450 isozymes.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of ophthalmic brinzolamide in pregnant women. Studies in animals have shown reproductive toxicity following systemic administration (see also section 5.3).

AZOPT is not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding

It is unknown whether brinzolamide/metabolites are excreted in human milk following topical ocular administration. Animal studies have shown the excretion of minimal levels of brinzolamide in breast milk following oral administration.

A risk to the newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from AZOPT therapy taking in to account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

Animal studies with brinzolamide demonstrated no effect on fertility. Studies have not been performed to evaluate the effect of topical ocular administration of brinzolamide on human fertility.

4.7 Effects on ability to drive and use machines

AZOPT has a minor 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 (see also section 4.8). If blurred vision occurs at instillation, the patient must wait until the vision clears before driving or using machines.

Oral carbonic anhydrase inhibitors may impair the ability to perform tasks requiring mental alertness and/or physical coordination (see also section 4.4 and section 4.8).

4.8 Undesirable effects

Summary of the safety profile

In clinical studies involving 2 732 patients treated with AZOPT as monotherapy or adjunctive therapy to timolol maleate 5 mg/ml, the most frequently reported treatment-related adverse reactions were: dysgeusia (6.0%) (bitter or unusual taste, see description below) and temporary blurred vision (5.4%) upon instillation, lasting from a few seconds to a few minutes (see also section 4.7).

Tabulated summary of adverse reactions

The following adverse reactions have been reported with brinzolamide 10mg/ml eye drops, suspension 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), or not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. The adverse reactions were obtained from clinical trials and post-marketing spontaneous reports.

System Organ Classification	**MedDRA Preferred Term (v.15.1)**
Infections and infestations	Uncommon: nasopharyngitis, pharyngitis, sinusitis Not Known: rhinitis
Blood and lymphatic system disorders	Uncommon: red blood cell count decreased, blood chloride increased
Immune system disorders	Not Known: hypersensitivity
Metabolism and nutrition disorders	Not known: decreased appetite
Psychiatric disorders	Uncommon: apathy, depression, depressed mood, libido decreased, nightmare, nervousness Rare: insomnia
Nervous system disorders	Uncommon: motor dysfunction, amnesia, dizziness, paraesthesia, headache Rare: memory impairment, somnolence Not Known: tremor, hypoaesthesia, ageusia
Eye disorders	Common: blurred vision, eye irritation, eye pain, foreign body sensation in eyes, ocular hyperaemia Uncommon: corneal erosion, keratitis, punctate keratitis, keratopathy, deposit eye, corneal staining, corneal epithelium defect, corneal epithelium disorder, blepharitis, eye pruritus, conjunctivitis, eye swelling, meibomianitis, glare, photophobiadry eye, allergic conjunctivitis, pterygium, scleral pigmentation, asthenopia, ocular discomfort, abnormal sensation in eye, keratoconjunctivitis sicca, subconjunctival cyst, conjunctival hyperaemia, eyelids pruritus, eye discharge, eyelid margin crusting, lacrimation increased Rare: corneal oedema, diplopia, visual acuity reduced, photopsia, hypoaesthesia eye, periorbital oedema, intraocular pressure increased, optic nerve cup/disc ratio increased Not Known: corneal disorder, visual disturbance, eye allergy, madarosis, eyelid disorder, erythema of eyelid
Ear and labyrinth disorders	Rare: tinnitus Not Known: vertigo
Cardiac disorders	Uncommon: cardio-respiratory distress, bradycardia, palpitations Rare: angina pectoris, heart rate irregular Not Known: arrhythmia, tachycardia, hypertension, blood pressure increased, blood pressure decreased, heart rate increased
Respiratory, thoracic and mediastinal disorders	Uncommon: dyspnoea, epistaxis, oropharyngeal pain, pharyngolaryngeal pain, throat irritation, upper airway cough syndrome, rhinorrhoea, sneezing Rare: bronchial hyperreactivity, upper respiratory tract congestion, sinus congestion, nasal congestion, cough, nasal dryness Not Known: asthma

Gastrointestinal disorders	Common: dysgeusia Uncommon: oesophagitis, diarrhoea, nausea, vomiting, dyspepsia, upper abdominal pain, abdominal discomfort, stomach discomfort, flatulence, frequent bowel movements, gastrointestinal disorder, hypoaesthesia oral, paraesthesia oral, dry mouth
Hepato-biliary disorders	Not Known: liver function test abnormal
Skin and subcutaneous tissue disorders	Uncommon: rash, rash maculo-papular, skin tightness Rare: urticaria, alopecia, pruritus generalised Not Known: Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) (see section 4.4), dermatitis, erythema
Musculoskeletal and connective tissue disorders	Uncommon: back pain, muscle spasms, myalgia Not Known: arthralgia, pain in extremity
Renal and urinary disorders	Uncommon: renal pain Not Known: pollakiuria
Reproductive system and breast disorders	Uncommon: erectile dysfunction
General disorders and administration site conditions	Uncommon: pain, chest discomfort, fatigue, feeling abnormal Rare: chest pain, feeling jittery, asthenia, irritability Not Known: peripheral oedema, malaise
Injury, poisoning and procedural complications	Uncommon: foreign body in eye

Description of selected adverse events

Dysgeusia (bitter or unusual taste in the mouth following instillation) was the most frequently reported systemic adverse reaction associated with the use of AZOPT during clinical studies. It is likely caused by passage of the eye drops in the nasopharynx via the nasolacrimal canal. Nasolacrimal occlusion or gently closing the eyelid after instillation may help reduce the incidence of this effect (see also section 4.2).

AZOPT is a sulphonamide inhibitor of carbonic anhydrase with systemic absorption. Gastrointestinal, nervous system, haematological, renal and metabolic effects are generally associated with systemic carbonic anhydrase inhibitors. The same type of adverse reactions that are attributable to oral carbonic anhydrase inhibitors may occur with topical administration.

No unexpected adverse reactions have been observed with AZOPT when used as adjunctive therapy to travoprost. The adverse reactions seen with the adjunctive therapy have been observed with each active substance alone.

Paediatric population

In small short-term clinical trials, approximately 12.5% of paediatric patients were observed to experience adverse reactions, the majority of which were local, non-serious ocular reactions such as conjunctival hyperaemia, eye irritation, eye discharge, and lacrimation increased (see also section 5.1).

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

No case of overdose has been reported.

Treatment should be symptomatic and supportive. Electrolyte imbalance, development of an acidotic state, and possible nervous system effects may occur. Serum electrolyte levels (particularly potassium) and blood pH levels must be monitored.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiglaucoma preparations and miotics, carbonic anhydrase inhibitors, ATC code: S01EC04

Mechanism of action

Carbonic anhydrase (CA) is an enzyme found in many tissues of the body, including the eye. Carbonic anhydrase catalyses the reversible reaction involving the hydration of carbon dioxide and the dehydration of carbonic acid.

Inhibition of carbonic anhydrase in the ciliary processes of the eye decreases aqueous humour secretion, presumably by slowing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport. The result is a reduction in intraocular pressure (IOP) which is a major risk factor in the pathogenesis of optic nerve damage and glaucomatous visual field loss. Brinzolamide, an inhibitor of carbonic anhydrase II (CA-II), the predominant iso-enzyme in the eye, with an *in vitro* IC_{50} of 3.2 nM and a K_i of 0.13 nM against CA-II.

Clinical efficacy and safety

The IOP-reducing effect of AZOPT as adjunctive therapy to the prostaglandin analogue travoprost was studied. Following a 4 week run-in with travoprost, patients with an IOP ≥19 mmHg were randomized to receive added treatment with brinzolamide or timolol. An additional decrease in mean diurnal IOP of 3.2 to 3.4 mmHg for the brinzolamide group and 3.2 to 4.2 mmHg for the timolol group were observed. There was an overall higher incidence of non-serious ocular adverse reactions, mainly related to signs of local irritation, in the brinzolamide/travoprost groups. The events were mild and did not affect the overall discontinuation rates in the studies (see also section 4.8).

A clinical trial was conducted with AZOPT in 32 paediatric patients less than 6 years of age, diagnosed with glaucoma or ocular hypertension. Some patients were naive to IOP therapy whilst others were on other IOP-lowering medicinal product(s). Those who had been on previous IOP medicinal product(s) were not required to discontinue their IOP medicinal product(s) until initiation of monotherapy with AZOPT.

Among patients who were naive to IOP therapy (10 patients), the efficacy of AZOPT was similar to that seen previously in adults, with mean IOP reductions from baseline ranging up to 5 mmHg. Among patients who were on topical IOP-lowering medicinal product(s) (22 patients), mean IOP increased slightly from baseline in the AZOPT group.

5.2 Pharmacokinetic properties

Following topical ocular administration, brinzolamide is absorbed into the systemic circulation. Due to its high affinity for CA-II, brinzolamide distributes extensively into the red blood cells (RBCs) and exhibits a long half-life in whole blood (mean of approximately 24 weeks). In humans, the metabolite N-desethylbrinzolamide is formed, which also binds to CA and accumulates in RBCs. This metabolite binds mainly to CA-I in the presence of brinzolamide. In plasma, both brinzolamide and N-desethylbrinzolamide concentrations are low and generally below assay quantitation limits (<7.5 ng/ml).

Binding to plasma proteins is not extensive (about 60%). Brinzolamide is eliminated primarily by renal excretion (approximately 60%). About 20% of the dose has been accounted for in urine as metabolite. Brinzolamide and N-desethylbrinzolamide are the predominant components in the urine along with trace levels (<1%) of the N-desmethoxypropyl and O-desmethyl metabolites.

In an oral pharmacokinetic study, healthy volunteers received 1 mg capsules of brinzolamide twice daily for up to 32 weeks and RBC CA activity was measured to assess the degree of systemic CA inhibition.

Brinzolamide saturation of RBC CA-II was achieved within 4 weeks (RBC concentrations of approximately 20 µM). N-Desethylbrinzolamide accumulated in RBCs to steady state within 20-28 weeks reaching concentrations ranging from 6-30 µM. The inhibition of total RBC CA activity at steady state was approximately 70-75%.

Subjects with moderate renal impairment (creatinine clearance of 30-60 ml/minute) were administered 1 mg of brinzolamide twice daily orally for up to 54 weeks. Brinzolamide RBC concentration ranged from about 20 to 40 µM by week 4 of treatment. At steady-state, brinzolamide and its metabolite RBC concentrations ranged from 22.0 to 46.1 and 17.1 to 88.6 µM, respectively.

N-desethylbrinzolamide RBC concentrations increased and total RBC CA activity decreased with decreasing creatinine clearance but brinzolamide RBC concentrations and CA-II activity remained unchanged. In subjects with the highest degree of renal impairment inhibition of total CA activity was greater although it was inferior to 90% at steady-state.

In a topical ocular study, at steady-state, brinzolamide RBC concentrations were similar to those found in the oral study, but levels of N-desethylbrinzolamide were lower. Carbonic anhydrase activity was approximately 40-70% of predose levels.

5.3 Preclinical safety data

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

Developmental toxicity studies in rabbits with oral doses of brinzolamide of up to 6 mg/kg/day (125 times the recommended human ophthalmic dose) revealed no effect on foetal development despite significant maternal toxicity. Similar studies in rats resulted in slightly reduced ossification of skull and sternebrae of foetuses of dams receiving brinzolamide at doses of 18 mg/kg/day (375 times the recommended human ophthalmic dose), but not 6 mg/kg/day. These findings occurred at doses that caused metabolic acidosis with decreased body weight gain in dams and decreased foetal weights. Dose-related decreases in foetal weights were observed in pups of dams receiving brinzolamide orally ranging from a slight decrease (about 5-6%) at 2 mg/kg/day to nearly 14% at 18 mg/kg/day. During lactation, the no adverse effect level in the offspring was 5 mg/kg/day.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzalkonium chloride
Mannitol (E421)
Carbomer 974P
Tyloxapol
Edetate disodium
Sodium chloride
Hydrochloric acid/sodium hydroxide (to adjust pH)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

2 years.

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

5 and 10 ml opaque low density polyethylene bottles with polypropylene screw caps.

The following pack sizes are available: outer cartons containing 1 x 5 ml, 3 x 5 ml and 1 x 10 ml bottles. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBERS

EU/1/00/129/001-3

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9 March 2000
Date of latest renewal: 29 January 2010

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 responsible for batch release

Novartis Pharma GmbH
Roonstraße 25
D-90429 Nuremberg
Germany

Novartis Manufacturing NV
Rijksweg 14
2870 Puurs-Sint-Amands
Belgium

Novartis Farmacéutica, S.A.
Gran Via de les Corts Catalanes, 764
08013 Barcelona
Spain

Siegfried El Masnou, S.A.
Camil Fabra 58
El Masnou
08320 Barcelona
Spain

Novartis Pharma GmbH
Sophie-Germain-Strasse 10
90443 Nuremberg
Germany

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

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, 5 ml, 10 ml + CARTON FOR 3 x 5 ml BOTTLES

1. NAME OF THE MEDICINAL PRODUCT

AZOPT 10 mg/ml eye drops, suspension
brinzolamide

2. STATEMENT OF ACTIVE SUBSTANCE

Each ml of suspension contains 10 mg of brinzolamide.

3. LIST OF EXCIPIENTS

Contains benzalkonium chloride, mannitol (E421), carbomer 974P, tyloxapol, edetate disodium, sodium chloride, hydrochloric acid/sodium hydroxide (to adjust pH) and purified water. See the package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Eye drops, suspension

5 ml
10 ml
3 x 5ml

5. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.
Shake well 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 four 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/1/00/129/001	1 x 5 ml
EU/1/00/129/002	1 x 10 ml
EU/1/00/129/003	3 x 5 ml

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16 INFORMATION IN BRAILLE

azopt

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, 5 ml & 10 ml

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

AZOPT 10 mg/ml eye drops, suspension
brinzolamide
Ocular use

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.
Discard 4 weeks after first opening.
Opened:

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

5 ml
10 ml

6 OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

AZOPT 10 mg/ml eye drops, suspension
brinzolamide

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or your 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 AZOPT is and what it is used for

AZOPT contains brinzolamide which belongs to a group of medicines called carbonic anhydrase inhibitors. It reduces pressure within the eye.

AZOPT eye drops are used to treat high pressure in the eye. This pressure can lead to an illness called glaucoma.

If the pressure in the eye is too high, it can damage your sight.

2. What you need to know before you use AZOPT

Do not use AZOPT
- if you have severe kidney problems.
- if you are allergic to brinzolamide or any of the other ingredients of this medicine (listed in section 6).
- if you are allergic to medicines called sulphonamides. Examples include medicines used to treat diabetes and infections and also diuretics (water tablets). AZOPT may cause the same allergy.
- if you have too much acidity in your blood (a condition called hyperchloraemic acidosis).

If you have further questions, ask your doctor for advice.

Warnings and precautions
Talk to your doctor or pharmacist before using AZOPT:
- if you have kidney or liver problems.
- if you have dry eyes or cornea problems.
- if you are taking other sulphonamide medicines
- if you have a specific form of glaucoma in which the pressure inside the eye rises due to deposits that block fluid draining out (pseudoexfoliative glaucoma or pigmentary glaucoma) or a specific form of glaucoma in which the pressure inside the eye (sometimes rapidly) rises because the eye bulges forward and blocks fluid draining out (narrow-angle glaucoma)
- if you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after using AZOPT or other related medicines.

Take special care with AZOPT:
Serious skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in association with brinzolamide treatment. Stop using AZOPT and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

Children and adolescents
AZOPT is not to be used by infants, children or adolescents under 18 years of age unless advised by your doctor.

Other medicines and AZOPT
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

If you are taking another carbonic anhydrase inhibitor (acetazolamide or dorzolamide, see section 1 What AZOPT is and what it is used for), talk to your doctor.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Women who may become pregnant are advised to use effective contraception during AZOPT treatment. The use of AZOPT is not recommended during pregnancy or breast-feeding. Do not use AZOPT unless clearly indicated by your doctor.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
Do not drive or use machines until your vision is clear. You may find that your vision is blurred for a time just after using AZOPT.

AZOPT may impair the ability to perform tasks requiring mental alertness and/or physical coordination. If affected, take care when driving or using machines.

AZOPT contains benzalkonium chloride

This medicine contains 3.35 µg benzalkonium chloride per drop (= 1 dose) which is equivalent to 0.01% or 0.1 mg/ml.

AZOPT contains a preservative (benzalkonium chloride) which may be absorbed by soft contact lenses and may change the colour of the contact lenses. You should remove contact lenses before using this medicine and put them back 15 minutes afterwards. Benzalkonium chloride may also cause eye irritation, especially if you have dry eyes or disorders of the cornea (the clear layer at the front of the eye). If you feel abnormal eye sensation, stinging or pain in the eye after using this medicine, talk to your doctor.

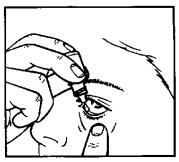
3. How to use AZOPT

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

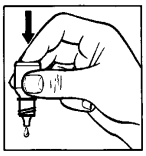
Only use AZOPT for your eyes. Do not swallow or inject.

The recommended dose is
1 drop in the affected eye or eyes twice a day - morning and night.
Use this much unless your doctor told you to do something different. Only use AZOPT in both eyes if your doctor told you to. Take it for as long as your doctor told you to.

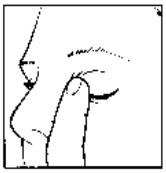
How to use



1



2



3

- Get the AZOPT bottle and a mirror
- Wash your hands
- Shake the bottle and twist off the cap. After the cap is removed, if the tamper evident snap collar is loose, remove before using product.
- Hold the bottle, pointing down, between your thumb and middle finger
- Tilt your head back. Pull down your eyelid with a clean finger, until there is a ‘pocket’ between the eyelid and your eye. The drop will go in here (picture 1)
- Bring the bottle tip close to the eye. Use the mirror if it helps
- Do not touch your eye or eyelid, surrounding areas or other surfaces with the dropper. It could infect the drops
- Gently press on the base of the bottle to release one drop of AZOPT at a time.
- Do not squeeze the bottle: it is designed so that a gentle press on the bottom is all that it needs (picture 2)
- After using AZOPT, press a finger to the corner of your eye, by the nose (picture 3) for at least 1 minute. This helps to stop AZOPT getting into the rest of the body.
- If you take drops in both eyes, repeat the steps for your other eye.
- Put the bottle cap back on firmly immediately after use
- Use up one bottle before opening the next bottle.

If a drop misses your eye, try again.

If you are using other eye drops, leave at least 5 minutes between putting in AZOPT and the other drops. Eye ointments should be administered last.

If you use more AZOPT than you should
If you get too much in your eyes, rinse it all out with warm water. Do not put in any more drops until it’s time for your next regular dose.

If you forget to use AZOPT
Use a single drop as soon as you remember, and then go back to your regular routine. Do not use a double dose to make up for a forgotten dose.

If you stop using AZOPT
If you stop using AZOPT without speaking to your doctor, the pressure in your eye will not be controlled which could lead to loss of sight.

4. Possible side effects

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

The following side effects have been seen with AZOPT.

Stop using AZOPT and seek medical attention immediately if you notice any of the following symptoms:
- reddish non-elevated, target-like or circular patches on the trunk, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome, toxic epidermal necrolysis).

Common *(may affect up to 1 in 10 people)*

- **Effects in the eye**: blurred vision, eye irritation, eye pain, eye discharge, itchy eye, dry eye, abnormal eye sensation, redness of the eye.

- **General side effects**: bad taste.

Uncommon *(may affect up to 1 in 100 people)*

- **Effects in the eye**: sensitivity to light, inflammation or infection of the conjunctiva, eye swelling, eyelid itching, redness or swelling, deposits in eye, glare, burning sensation, growth on surface of eye, increased pigmentation of the eye, tired eyes, eyelid crusting, or increased tear production.

- **General side effects**: decreased or reduced heart function, a forceful heartbeat that may be rapid or irregular, decreased heart rate, difficulty breathing, shortness of breath, cough, decreased red blood cell count in blood, increased chlorine level in blood, dizziness, difficulty with memory, depression, nervousness, decreased emotional interest, nightmare, generalized weakness, fatigue, feeling abnormal, pain, movement problems, decreased sex drive, male sexual difficulty, cold symptoms, chest congestion, sinus infection, throat irritation, throat pain, abnormal or decreased sensation in mouth, inflammation of the lining of the oesophagus, abdominal pain, nausea, vomiting, upset stomach, frequent bowel movements, diarrhoea, intestinal gas, digestive disorder, kidney pain, muscle pain, muscle spasms, back pain, nose bleeds, runny nose, stuffy nose, sneezing, rash, abnormal skin sensation, itching, smooth skin rash or redness covered by elevated bumps, skin tightness, headache, dry mouth, debris in eye.

Rare *(may affect up to 1 in 1 000 people)*

- **Effects in the eye**: corneal swelling, double or reduced vision, abnormal vision, flashes of light in the field of vision, decreased eye sensation, swelling around the eye, increased pressure in eye, damage to the optic nerve.

- **General side effects**: memory impairment, drowsiness, chest pain, upper respiratory tract congestion, sinus congestion, nasal congestion, dry nose, ringing in ears, hair loss, generalized itching, feeling jittery, irritability, irregular heart rate, body weakness, difficulty sleeping, wheezing, itchy skin rash.

Not known (*frequency cannot be estimated from the available data*)

- **Effects in the eye**: eyelid abnormality, visual disturbance, corneal disorder, eye allergy, decreased growth or number of eyelashes, eyelid redness.

- **General side effects**: increased allergic symptoms, decreased sensation, tremor, loss or decrease in taste, decreased blood pressure, increased blood pressure, increased heart rate, joint pain, asthma, pain in extremity, skin redness, inflammation, or itching, abnormal liver blood tests, swelling of the extremities, frequent urination, decreased appetite, feeling unwell, reddish non-elevated, target-like or circular patches on the trunk, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes, which can be preceded by fever and flu-like symptoms. These serious skin rashes can be potentially life-threatening (Stevens-Johnson syndrome, toxic epidermal necrolysis).

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 AZOPT

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 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 a bottle four weeks after you first opened it, to prevent infections. Write down the date you opened each bottle in the space below and in the space on the bottle label and box. For a pack containing a single bottle, write only one date.

Opened (1):
Opened (2):
Opened (3):

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

6 Contents of the pack and other information

What AZOPT contains

- The active substance is brinzolamide. Each millilitre contains 10 mg of brinzolamide.
- The other ingredients are benzalkonium chloride, carbomer 974P, edetate disodium, mannitol (E421), purified water, sodium chloride, tyloxapol. Tiny amounts of hydrochloric acid or sodium hydroxide are added to keep acidity levels (pH levels) normal.

What AZOPT looks like and contents of the pack
AZOPT is a milky liquid (a suspension) supplied in a pack containing a 5 ml or a 10 ml plastic bottle with a screw cap, or in a pack containing three 5 ml plastic bottles with screw caps. Not all pack sizes may be marketed.

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