BRINZOX Brinzolamide Ophthalmic Suspension USP 1 % w/v	
Module 1	Administrative Information and Product Information
Section 1.6	Product Information

1.6.3 Patient Information Leaflet (PIL)

Please find enclosed herewith Package Insert.

Front

TN47241

BRINZOX

Brinzolamide Ophthalmic
Suspension USP 1.0% w/v
EYE DROPS

Composition :

Brinzolamide USP	1.0% w/v
Benzalkonium Chloride USPNF (As preservative)	0.01% w/v
Sterile Aqueous base	q.s.

Pharmaceutical Form :
Ophthalmic Suspension (Eye drops)

White to off-white coloured, aqueous suspension.

List of Excipients :
Benzalkonium Chloride USPNF, Tyloxapol USP, Carbomer Homopolymer USPNF, Mannitol BP, Disodium Edetate BP, Sodium Chloride BP, Sodium Hydroxide BP (Pellets), Water for Injection IP/BP/USP/IH

Clinical Particulars
Therapeutic Indications :
Brinzolamide is a carbonic anhydrase inhibitor indicated in the treatment of elevated intraocular pressure (IOP) in patients with ocular hypertension or open-angle glaucoma.

Dosage and Administration :
The recommended dose is one drop of Brinzolamide in the affected eye(s) 3 times daily. Brinzolamide may be used concomitantly with other topical ophthalmic drug products to lower IOP. If more than one topical ophthalmic drug is being used, the drugs should be administered at least 10 minutes apart.

Contraindications :
Brinzolamide is contraindicated in patients who are hypersensitive to any component of this product.

Warning and Precautions :
Sulfonamide Hypersensitivity Reactions
Brinzolamide is a sulfonamide and although administered topically, it is absorbed systemically. Therefore, the same types of adverse reactions that are attributable to sulfonamides may occur with topical administration of Brinzolamide. Fatalities have occurred, although rarely, due to severe reactions to sulfonamides, including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias. Sensitization may recur when a sulfonamide is re-administered irrespective of the route of administration. If signs of serious reactions or hypersensitivity occur, discontinue the use of this preparation.

Corneal Endothelium
Carbonic anhydrase activity has been observed in both the cytoplasm and around the plasma membranes of the corneal endothelium. There is an increased potential for developing corneal edema in patients with low endothelial cell counts. Caution should be used when prescribing Brinzolamide to this group of patients.

Severe Renal Impairment
Brinzolamide has not been studied in patients with severe renal impairment [creatinine clearance (CrCl) less than 30 mL/min]. Because Brinzolamide and its metabolite are excreted predominantly by the kidney, Brinzolamide is not recommended in such patients.

Acute Angle-Closure Glaucoma
The management of patients with acute angle-closure glaucoma requires therapeutic interventions in addition to ocular hypotensive agents. Brinzolamide has not been studied in patients with acute angle-closure glaucoma.

Risk of Contamination
Avoid allowing the tip of the dispensing container to contact the eye or surrounding structures or other surfaces, since the product 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 contaminated solutions.

Contact Lens Wear
The preservative in Brinzolamide, benzalkonium chloride, may be absorbed by soft contact lenses. Contact lenses should be removed during instillation of Brinzolamide, but may be reinserted 15 minutes after instillation.

Drug Interactions :
Oral Carbonic Anhydrase Inhibitors
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 Brinzolamide. The concomitant administration of Brinzolamide and oral carbonic anhydrase inhibitors is not recommended.

High-Dose Salicylate Therapy
Carbonic anhydrase inhibitors may produce acid-base and electrolyte alterations. These alterations were not reported in the clinical trials with brinzolamide. However, in patients treated with oral carbonic anhydrase inhibitors, rare instances of acid-base alterations have occurred with high-dose salicylate therapy. Therefore, the potential for such drug interactions should be considered in patients receiving Brinzolamide.

Pregnancy and Lactation :
Pregnancy
There are no adequate and well-controlled studies in pregnant women to inform drug-associated risk.
In reproductive toxicity studies, brinzolamide administered orally to rats induced fetal toxicity at 375-times the recommended human ophthalmic dose (RHOD) based on mg/kg. In rabbits, no fetal toxicity was observed following oral administration.

Lactation
There are no data on the presence of brinzolamide in human milk, the effects on the breastfed infant, or the effects on milk production. Brinzolamide has been detected in the milk of lactating rats.
The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for brinzolamide and any potential adverse effects on the breast-fed child from brinzolamide.

Adverse Reactions :
Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to the rates in the clinical trials of another drug and may not reflect the rates observed in practice.
In clinical studies of Brinzolamide, the most frequently reported adverse reactions reported in 5% to 10% of patients were blurred vision and bitter, sour or unusual taste. Adverse reactions occurring in 1% to 5% of patients were blepharitis, dermatitis, dry eye, foreign body sensation, headache, hyperemia, ocular discharge, ocular discomfort, ocular keratitis, ocular pain, ocular pruritus, and rhinitis.
The following adverse reactions were reported at an incidence below 1%: allergic reactions, alopecia, chest pain, conjunctivitis, diarrhea, diplopia, dizziness, dry mouth, dyspnea, dyspepsia, eye fatigue, hypertonia, keratoconjunctivitis, keratopathy, kidney pain, lid margin crusting or sticky sensation, nausea, pharyngitis, tearing, and urticaria.

Overdosage :
Although no human data are available, electrolyte imbalance, development of an acidotic state, and possible nervous system effects may occur following oral administration of an overdose. Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored.

Clinical Pharmacology
Mechanism of Action
Carbonic anhydrase is an enzyme found in many tissues of the body, including the eye. It catalyzes the reversible reaction involving the hydration of carbon dioxide and the dehydration of carbonic acid. In humans, carbonic anhydrase exists as a number of isoenzymes, the most active being carbonic anhydrase II, found primarily in red blood cells (RBCs), but also in other tissues. Inhibition of carbonic anhydrase in the ciliary processes of the eye decreases aqueous humor secretion, presumably by slowing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport. The result is a reduction in IOP.
Brinzox contains brinzolamide, an inhibitor of carbonic anhydrase II. Following topical ocular administration, brinzolamide inhibits aqueous humor formation and reduces elevated IOP. Elevated IOP is a major risk factor in the pathogenesis of optic nerve damage and glaucomatous visual field loss.

Pharmacokinetics :
Following topical ocular administration, brinzolamide is absorbed into the systemic circulation. Due to its affinity for carbonic anhydrase II, brinzolamide distributes extensively into the RBCs and exhibits a long half-life in whole blood (approximately 111 days). In humans, the metabolite N-desethyl brinzolamide is formed, which also binds to carbonic anhydrase and accumulates in RBCs. This metabolite binds mainly to carbonic anhydrase I in the presence of brinzolamide. In plasma, both parent brinzolamide and N-desethyl brinzolamide concentrations are low and generally below assay quantitation limits (less than 10 ng/mL). Binding to plasma proteins is approximately 60%. Brinzolamide is eliminated predominantly in the urine as unchanged drug. N-Desethyl brinzolamide is also found in the urine along with lower concentrations of the N-desmethoxypropyl and O-desmethyl metabolites.

An oral pharmacokinetic study was conducted in which healthy volunteers received 1 mg capsules of brinzolamide twice per day for up to 32 weeks. This regimen approximates the amount of drug delivered by topical ocular administration of brinzolamide dosed to both eyes 3 times per day and simulates systemic drug and metabolite concentrations similar to those achieved with long-term topical dosing. Red blood cell carbonic anhydrase activity was measured to assess the degree of systemic carbonic anhydrase inhibition. Brinzolamide saturation of RBC carbonic anhydrase II was achieved within 4 weeks (RBC concentrations of approximately 20 mcM). N-Desethyl brinzolamide accumulated in RBCs to steady-state within 20 to 28 weeks reaching concentrations ranging from 6 to 30 mcM. The inhibition of carbonic anhydrase II activity at steady state was approximately 70% to 75%, which is below the degree of inhibition expected to have a pharmacological effect on renal function or respiration in healthy subjects.

Preclinical Safety data :
Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis
Brinzolamide caused urinary bladder tumors in female mice at oral doses of 10 mg/kg/day and in male rats at oral doses of 8 mg/kg/day in 2-year studies. Brinzolamide was not carcinogenic in male mice or female rats dosed orally for up to 2 years. The carcinogenicity appears secondary to kidney and urinary bladder toxicity. These levels of exposure cannot be achieved with topical ophthalmic dosing in humans.

Mutagenesis
The following tests for mutagenic potential were negative: (1) *in vivo* mouse micronucleus assay; (2) *in vivo* sister chromatid exchange assay; and (3) Ames *E. coli* test. The *in vitro* mouse lymphoma forward mutation assay was negative in the absence of activation, but positive in the presence of microsomal activation.

Impairment of Fertility
In reproduction studies of brinzolamide in rats, there were no adverse effects on the fertility or reproductive capacity of males or females at doses up to 18 mg/kg/day (375 times the RHOD based on mg/kg).

Pharmaceutical particularsIncompatibilities :
Not applicable

Shelf life : 36 Months

Special Precautions for storage : Use the suspension within four weeks after first opening.

Storage Condition : Do not store above 30ºC.

Nature and contents of container : 5 mL vial packed in a carton along with pack insert.

Marketing Authorization Holder :

Manufacturing Site :	Registered office:
Ajanta Pharma Ltd. Mirza - Palashbhari Road, Village Kokhjar, Kamrup (R), Guwahati, Assam – 781128	Ajanta House, Charkop, Kandivli (W), Mumbai 400 067 India.

Date of revision of text : Dec 2021

Pharma Code : 100000 Minicode

Direction for Travel

Date	: 15.02.2022
Artist	: Ganesh
Product	: Brinzox Eye Drops 5ml
Actual Size	: 350 x 210 mm
Ref artwork	: 3027062
Colour	: Black
Country	: Anglo Africa

Back

BRINZOX
EYE DROPS

BRINZOLAMIDE OPHTHALMIC
SUSPENSION USP 1.0% W/V

Patient Information Leaflet

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.

What is in this leaflet?

1. What Brinzox is and what it is used for

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

Brinzox is 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 Brinzox

Do not use Brinzox

- If you have severe kidney problems.
- If you are allergic to Brinzolamide or any of the other ingredients of this medicine
- If you are allergic to medicines called Sulphonamides. Examples include medicines used to treat diabetes and infections and also diuretics (water tablets). Brinzox 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 Brinzox:

- 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)

Children and adolescents

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

Other medicines and Brinzox

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), 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 Brinzox treatment. The use of Brinzox is not recommended during pregnancy or breast-feeding. Do not use B Brinzox 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 Brinzox.

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

Brinzox contains Benzalkonium Chloride

Brinzox 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 Brinzox

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 Brinzox 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 Brinzox in both eyes if your doctor told you to. Take it for as long as your doctor told you to.

If you use more Brinzox 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 Brinzox

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 Brinzox

If you stop using Brinzox 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 Brinzox.

Common side effects

(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 side effects
(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 side effects

(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.

5. How to store Brinzox

- Keep this medicine out of the sight and reach of children.
- Do not store above 30°C.
- 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.
- Use the suspension within one month after opening the vial.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Brinzox contains:

The active substance is: Brinzolamide USP(1.0% w/v)

List of excipients: Benzalkonium Chloride USPNF, Tyloxapol USP, Carbomer Homopolymer (Type –B) USPNF, Mannitol BP, Disodium Edetate BP, Sodium Chloride BP, Sodium Hydroxide BP and Water for Injections BP / USP.

What Brinzox looks like and contents of the pack

White to off-white coloured, aqueous suspension.
5 mL suspension in LDPE vial packed in a carton along with pack insert.

SUPPLIER AND MANUFACTURER

Supplier	Manufacturer
Ajanta Pharma Limited Ajanta House, Charkop Kandivli (West) Mumbai - 400 067 India.	Ajanta Pharma Limited Mirza-Palashbari Road, Village Kokjhar, Kamrup (R), Guwahati, Assam - 781128.

For any information about this medicinal product, please contact the Supplier.

DATE OF PUBLICATION OR REVISION
Dec, 2021

BRINZOX

(Brinzolamide Ophthalmic Suspension USP 1.0% w/v)

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