SUMMARY OF PRODUCT CHARACTERISTICS

1.	**Name of the Medical Product**
	1.1 Product Name : Bimat (Bimatoprost Ophthalmic Solution 0.03% w/v)
	1.2 Strength : Each ml contains Bimatoprost …… 0.3 mg
	1.3 Pharmaceutical Dosage Form : Eye drops
2.	**Qualitative & Quantitative Composition:** Each ml contains Bimatoprost …… 0.3 mg Benzalkonium Chloride USP/NF… 0.005% w/v (As preservative) Sterile aqueous vehicle q.s. For a full list of excipients, see section 6.1 of SmPC
3.	**Pharmaceutical Form:**
	Ophthalmic Solution (Eye drops) Clear, colourless solution, free from particulate matter.
4.	**Clinical Particulars**
	4.1 Therapeutic Indications: Bimatoprost Ophthalmic Solution, 0.03% is indicated for the reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension.
	4.2 Posology and Method of administration: The recommended dosage is one drop in the affected eye(s) once daily in the evening. Bimatoprost ophthalmic solution, 0.03% should not be administered more than once daily since it has been shown that more frequent administration of prostaglandin analogs may decrease the intraocular pressure lowering effect. Reduction of the intraocular pressure starts approximately 4 hours after the first administration with maximum effect reached within approximately 8 to 12 hours. Bimatoprost ophthalmic solution, 0.03% may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

	Pediatric Use Use in pediatric patients below the age of 16 years is not recommended because of potential safety concerns related to increased pigmentation following long-term chronic use. **Geriatric Use** No overall clinical differences in safety or effectiveness have been observed between elderly and other adult patients. Method of administration *For ocular use.* If more than one topical ophtalmic medicinal product is being used, each one should be administered at least 5 minutes apart. 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: Bimatoprost Ophthalmic Solution, 0.03% is contraindicated in patients with hypersensitivity to bimatoprost or to any of the ingredients.
	4.4 Special warning and precautions for use: ***Pigmentation*** Bimatoprost Ophthalmic Solution has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid) and eyelashes. Pigmentation is expected to increase as long as bimatoprost is administered. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of bimatoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long term effects of increased pigmentation are not known. Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with bimatoprost ophthalmic solution, 0.03% can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly. ***Eyelash Changes*** Bimatoprost Ophthalmic Solution, 0.03% may gradually change eyelashes and vellus hair in the treated eye. These changes include increased length, thickness, and number of

	lashes. Eyelash changes are usually reversible upon discontinuation of treatment. ***Intraocular Inflammation*** Prostaglandin analogs, including bimatoprost, have been reported to cause intraocular inflammation. In addition, because these products may exacerbate inflammation, caution should be used in patients with active intraocular inflammation (e.g., uveitis). ***Macular Edema*** Macular edema, including cystoid macular edema, has been reported during treatment with bimatoprost ophthalmic solution. Bimatoprost ophthalmic solution, 0.03% should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema. ***Bacterial Keratitis*** There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface. ***Use with Contact Lenses*** Bimatoprost Ophthalmic Solution, 0.03% contains benzalkonium chloride, which may be absorbed by and cause discoloration of soft contact lenses. Contact lenses should be removed prior to instillation of bimatoprost ophthalmic solution, 0.03% and may be reinserted 15 minutes following its administration.
	4.5 Interactions with other medicinal products and other forms of Interactions : No interaction studies have been performed. No interactions are anticipated in humans, since systemic concentrations of bimatoprost are extremely low (less than 0.2 ng/mL) following ocular dosing with bimatoprost 0.3 mg/mL eye drops, solution (multi-dose formulation). Bimatoprost is biotransformed by any of multiple enzymes and pathways, and no effects on hepatic drug metabolizing enzymes were observed in preclinical studies. In published clinical studies, bimatoprost was used concomitantly with a number of different ophthalmic beta-blocking agents without evidence of interactions. Concomitant use of bimatoprost and anti-glaucomatous agents other than topical beta-blockers has not been evaluated during adjunctive glaucoma therapy. There is a potential for the IOP-lowering effect of prostaglandin analogues to be reduced in patients with glaucoma or ocular hypertension when used with other prostaglandin analogues.

	4.6 Pregnancy and Lactation: ***Pregnancy*** There are no adequate and well-controlled studies of bimatoprost ophthalmic solution, 0.03% administration in pregnant women. There is no increase in the risk of major birth defects or miscarriages based on bimatoprost post-marketing experience. Because animal reproductive studies are not always predictive of human response bimatoprost ophthalmic solution, 0.03% should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus. ***Lactation*** It is not known whether topical ocular treatment with bimatoprost ophthalmic solution, 0.03% could result in sufficient systemic absorption to produce detectable quantities in human milk. In animal studies, bimatoprost has been shown to be present in breast milk of lactating rats at an intravenous dose (i.e., 1 mg/kg) 324 times the RHOD (on m^2 g/m basis), however no animal data is available at clinically relevant doses. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for bimatoprost ophthalmic solution, 0.03% and any potential adverse effects on the breastfed child from bimatoprost ophthalmic solution, 0.03%.
	4.7 Effects on ability to drive and use machine: Bimatoprost has negligible influence on the ability to drive and use machines. As with any ocular treatment, if transient blurred vision occurs at instillation, the patient should wait until the vision clears before driving or using machines.
	4.8 Undesirable Effects: The following adverse reactions are described elsewhere in the labeling: ***Clinical Trials Experience*** Because published clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. In published clinical trials, the most frequent events associated with the use of bimatoprost ophthalmic solution, 0.03% occurring in approximately 15% to 45% of patients, in descending order of incidence, included conjunctival hyperemia, growth of eyelashes, and ocular pruritus. Approximately 3% of patients discontinued therapy due to conjunctival hyperemia Ocular adverse events occurring in approximately 3 to 10% of patients, in descending order of incidence, included ocular dryness, visual disturbance, ocular burning, foreign body

	sensation, eye pain, pigmentation of the periocular skin, blepharitis, cataract, superficial punctate keratitis, periorbital erythema, ocular irritation, and eyelash darkening. The following ocular adverse events reported in approximately 1 to 3% of patients, in descending order of incidence, included: eye discharge, tearing, photophobia, allergic conjunctivitis, asthenopia, increases in iris pigmentation, and conjunctival edema. In less than 1% of patients, intraocular inflammation was reported as iritis. Systemic adverse events reported in approximately 10% of patients were infections (primarily colds and upper respiratory tract infections). The following systemic adverse events reported in approximately 1 to 5% of patients, in descending order of incidence, included headaches, abnormal liver function tests, asthenia and hirsutism. ***Post-marketing Experience*** The following adverse reactions have been identified during post approval use of bimatoprost ophthalmic solution, 0.03%. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to bimatoprost ophthalmic solution, or a combination of these factors, include: abnormal hair growth, asthma like symptoms, dizziness, dyspnea, eyelid edema, hypersensitivity reaction including signs and symptoms of eye allergy and allergic dermatitis, hypertension, nausea, and periorbital and lid changes including deepening of the eyelid sulcus.
	4.9 Overdosage: No information is available on overdosage in humans. If overdose with bimatoprost ophthalmic solution, 0.03% occurs, treatment should be symptomatic. In oral (by gavage) mouse and rat general toxicity studies, doses up to 100 mg/kg/day did not produce any toxicity. This dose expressed as mg/m^2 is at least 70 times higher than the accidental dose of one bottle of bimatoprost ophthalmic solution, 0.03% for a 10 kg child.
5.	**Pharmacological properties**
	5.1 Pharmacodynamic Properties: Pharmacotherapeutic group: Ophthalmologicals, prostaglandin analogues, ATC code: S01EE03. **Clinical Pharmacology** Bimatoprost ophthalmic solution, 0.03% is a synthetic prostamide analog with ocular hypotensive activity. **Mechanism of Action** Bimatoprost, a prostaglandin analog, is a synthetic structural analog of prostaglandin with ocular hypotensive activity. It selectively mimics the effects of naturally occurring

	substances, prostamides. Bimatoprost is believed to lower intraocular pressure (IOP) in humans by increasing outflow of aqueous humor through both the trabecular meshwork and uveoscleral routes. Elevated IOP presents a major risk factor for glaucomatous field loss. The higher the level of IOP, the greater the likelihood of optic nerve damage and visual field loss.
	5.2 Pharmacokinetics Properties: Absorption: After one drop of bimatoprost ophthalmic solution, 0.03% was administered once daily to both eyes of 15 healthy subjects for two weeks, blood concentrations peaked within 10 minutes after dosing and were below the lower limit of detection (0.025 ng/mL) in most subjects within 1.5 hours after dosing. Mean C_{max} and AUC_0 to $_{24hr}$ values were similar on days 7 and 14 at approximately 0.08 ng/mL and 0.09 ng•hr/mL, respectively, indicating that steady state was reached during the first week of ocular dosing. There was no significant systemic drug accumulation over time. Distribution: Bimatoprost is moderately distributed into body tissues with a steady-state volume of distribution of 0.67 L/kg. In human blood, bimatoprost resides mainly in the plasma. Approximately 12% of bimatoprost remains unbound in human plasma. Metabolism: Bimatoprost is the major circulating species in the blood once it reaches the systemic circulation following ocular dosing. Bimatoprost then undergoes oxidation, N-deethylation and glucuronidation to form a diverse variety of metabolites. Elimination: Following an intravenous dose of radiolabeled bimatoprost (3.12 mcg/kg) to six healthy subjects, the maximum blood concentration of unchanged drug was 12.2 ng/mL and decreased rapidly with an elimination half-life of approximately 45 minutes. The total blood clearance of bimatoprost was 1.5 L/hr/kg. Up to 67% of the administered dose was excreted in the urine while 25% of the dose was recovered in the feces.
	5.3 Preclinical Safety data: *Carcinogenesis, Mutagenesis, Impairment of Fertility* Carcinogenesis Bimatoprost was not carcinogenic in either mice or rats when administered by oral gavage for 104 weeks at doses of up to 2 mg/kg/day and 1 mg/kg/day respectively (at least 192 and 291 times the human systemic exposure at the RHOD, respectively, based on blood AUC levels). Mutagenesis Bimatoprost was not mutagenic or clastogenic in the Ames test, in the mouse lymphoma test, or in the in vivo mouse micronucleus tests. Impairment of Fertility Bimatoprost did not impair fertility in male or female rats at doses up to 0.6 mg/kg/day (at

	least 103 times the human systemic exposure at the RHOD, based on blood AUC levels).
6.	**Pharmaceutical particulars**
	6.1 List of Excipients: Benzalkonium Chloride, Potassium Dihydrogen Phosphate, Anhydrous Disodium Hydrogen Phosphate, Polyoxyl 40 Hydrogenated Castor Oil, Sodium Chloride, Hydrochloric Acid, Water for Injections.
	6.2 Incompatibilities: Not Applicable
	6.3 Shelf life: 2 Years (unopened). 4 weeks after first opening.
	6.4 Special Precautions for storage: Store below 30°C. Use this Solution within 4 weeks after opening the vial.
	6.5 Nature and contents of container: 3 mL solution in 5 mL LDPE vial. Such vial packed in a carton along with pack insert.
	6.6 Special precautions for disposal: Not applicable
7.	**Marketing Authorization Holder:** Ajanta Pharma Limited Ajanta House, Charkop, Kandivli (West), Mumbai- 400 067, India **Manufacturing Site Address:** At: Ciron Drugs & Pharmaceuticals Pvt. Ltd. N-118, 118/1, 119, 119/1, 119/2, 113 MIDC, Tarapur, Boisar, Dist. Thane 401506, Maharashtra State, India
8.	**Marketing Authorization Numbers:** Not applicable
9.	**Date of first registration /renewal of the registration:** Not Applicable
10.	**Date of revision of text:** Mar 03, 2020