Summary of Product Characteristics
(Product Data Sheet)

1.	**Name of the Medical Product**
	1.1 Product Name: **APDROPS** (Moxifloxacin Hydrochloride Eye Drops 0.5% w/v)
	1.2 Strength : Moxifloxacin Hydrochloride BP 5.45 mg Equivalent to Moxifloxacin base 5.00 mg Sterile aqueous vehicle q.s.
	1.3 Pharmaceutical Dosage Form : Ophthalmic Solution (Eye Drops)
2.	**Qualitative & Quantitative Composition:** Eack ml contains Moxifloxacin Hydrochloride BP 5.45 mg Equivalent to Moxifloxacin base 5.00 mg Sterile aqueous vehicle q.s For a full list of excipients, see section 6.1 of SmPC
3.	**Pharmaceutical Form:** Ophthalmic Solution (Eye Drops) Pale yellow coloured clear solution free from visible particles.
4.	**Clinical Particulars**
	4.1 Therapeutic Indications: Moxifloxacin Hydrochloride Eye Drops is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of the following organisms: **Aerobic Gram-positive microorganisms:** *Corynebacterium species, Micrococcus luteus, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis, Staphylococcus warneri, Streptococcus pneumoniae, Streptococcus viridans group* **Aerobic Gram-negative microorganisms:** *Acinetobacter lwoffi, Haemophilus influenza, Haemophilus parainfluenzae* **Other microorganisms:** *Chlamydia trachomatis*
	4.2 Posology and Method of administration: **Posology and Method of Administration** Use in adults including the elderly (≥ 65 years) The dose is one drop in the affected eye(s) 3 times a day. The infection normally improves within 5 days and treatment should then be continued for a further 2-3 days. If no improvement is observed within 5 days of initiating therapy, the diagnosis and/or treatment should be reconsidered. The duration of treatment depends on the severity of the disorder and on the clinical and bacteriological course of infection.

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	Paediatric patients No dosage adjustment is necessary. Use in hepatic and renal impairment No dosage adjustment is necessary. Method of administration For ocular use only. Not for injection. Moxifloxacin Hydrochloride Eye Drops, solution should not be injected subconjunctivally or introduced directly into the anterior chamber of the eye. 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. In order to prevent the drops from being absorbed via the nasal mucosa, particularly in new-born infants or children, the nasolacrimal ducts should be held closed for 2 to 3 minutes with the fingers after administering the drops. After cap is removed, if tamper evident snap collar is loose, remove before using the product. If more than one topical ophthalmic medicinal product is being used, the medicinal products must be administered at least 5 minutes apart. Eye ointments should be administered last.
	4.3 Contraindications: Moxifloxacin solution is contraindicated in patients with a history of hypersensitivity to moxifloxacin, to other quinolones, or to any of the components in this medication.
	4.4 Special warning and precautions for use: **Special warning and precaution for use** In patients receiving systemically administered quinolones, serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported, some following the first dose. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial oedema), airway obstruction, dyspnoea, urticaria, and itching. If an allergic reaction to Moxifloxacin Hydrochloride Eye Drops occurs, discontinue use of the medicinal product. Serious acute hypersensitivity reactions to moxifloxacin or any other product ingredient may require immediate emergency treatment. Oxygen and airway management should be administered where clinically indicated. As with other anti-infectives, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue use and institute alternative therapy. Tendon inflammation and rupture may occur with systemic fluoroquinolone therapy including moxifloxacin, particularly in older patients and those treated concurrently with corticosteroids. Following ophthalmic administration of Moxifloxacin Hydrochloride Eye Drops plasma concentrations of moxifloxacin are much lower than after therapeutic oral doses of moxifloxacin however, caution should be exercised and treatment with Moxifloxacin Hydrochloride Eye Drops should be discontinued at the first sign of tendon inflammation Moxifloxacin Hydrochloride Eye Drops should not be used for the prophylaxis or empiric treatment of gonococcal conjunctivitis, including gonococcalophthalmia neonatorum, because of the prevalence of fluoroquinolone-resistant Neisseria gonorrhoeae. Patients with eye infections caused by Neisseria gonorrhoeae should receive appropriate systemic

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	treatment. Patients should be advised not to wear contact lenses if they have signs and symptoms of a bacterial ocular infection. Paediatric population Data are very limited to establish efficacy and safety of Moxifloxacin Hydrochloride Eye Drops in the treatment of conjunctivitis in neonates. Therefore use of this medicinal product to treat conjunctivitis in neonates is not recommended. Neonates with ophthalmia neonatorum should receive appropriate treatment for their condition, e.g. systemic treatment in cases caused by Chlamydia trachomitis or Neisseria gonorrhoeae. The medicinal product is not recommended for the treatment of Chlamydia trachomatis in patients less than 2 years of age as it has not been evaluated in such patients. Patients older than 2 years of age with eye infections caused by Chlamydia trachomitis should receive appropriate systemic treatment.
	4.5 Interactions with other medicinal products and other forms of Interactions : In vitro studies indicate that moxifloxacin does not inhibit CYP3A4, CYP2D6, CYP2C9, CYP2C19, or CYP1A2, indicating that moxifloxacin is unlikely to alter the pharmacokinetics of drugs metabolized by these cytochrome P450 isozymes.
	4.6 Pregnancy and Lactation: **Pregnancy** There are no or limited amount of data from the use of Moxifloxacin Hydrochloride Eye Drops in pregnant women. However, no effects on pregnancy are anticipated since the systemic exposure to moxifloxacin is negligible. The medicinal product can be used during pregnancy. **Breastfeeding** It is unknown whether moxifloxacin/metabolites are excreted in human milk. Animal studies have shown excretion of low levels in breast milk after oral administration of moxifloxacin. However, at therapeutic doses of Moxifloxacin Hydrochloride Eye Drops no effects on the suckling child are anticipated. The medicinal product can be used during breast-feeding. **Fertility** Studies have not been performed to evaluate the effect of ocular administration of Moxifloxacin Hydrochloride Eye Drops on fertility.
	4.7 Effects on ability to drive and use machine: Moxifloxacin has no or negligible influence on the ability to drive and use machines, however, as with any eye drops, temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs at instillation, the patient should wait until their vision clears before driving or using machinery.

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4.8 Undesirable Effects:

Summary of the safety profile

In clinical studies involving 2,252 patients, Moxifloxacin Hydrochloride Eye Drops was administered up to 8 times a day, with over 1,900 of these patients receiving treatment 3 times daily. The overall safety population that received the medicinal product consisted of 1,389 patients from the United States and Canada, 586 patients from Japan and 277 patients from India. No serious ophthalmic or systemic undesirable effects related to the medicinal product were reported in any of the clinical studies. The most frequently reported treatment-related undesirable effects with the medicinal product were eye irritation and eye pain, occurring at an overall incidence of 1 to 2%. These reactions were mild in 96% of those patients who experienced them, with only 1 patient discontinuing therapy as a result.

Tabulated summary of adverse reactions

The following adverse reactions 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, undesirable effects are presented in decreasing order of seriousness.

System Organ Classification	Frequency	Adverse reactions
Blood and lymphatic system disorders	Rare	haemoglobin decreased
Immune system disorders	Not known	Hypersensitivity
Nervous system disorders	Uncommon Rare Not known	headache paresthesia dizziness
Eye disorders	Common Uncommon Rare Not known	eye pain, eye irritation punctate keratitis, dry eye, conjunctival haemorrhage, ocular hyperaemia, eye pruritus, eyelid oedema, ocular discomfort, corneal epithelium defect, corneal disorder, conjunctivitis, blepharitis, eye swelling, conjunctival oedema, vision blurred, visual acuity reduced, asthenopia, erythema of eyelid endophthalmitis, ulcerative keratitis, corneal erosion, corneal abrasion, intraocular pressure increased, corneal opacity, corneal infiltrates, corneal deposits, eye allergy, keratitis, corneal oedema, photophobia, eyelid oedema, lacrimation increased, eye discharge,

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		foreign body sensation in eyes
Cardiac disorders	Not known	palpitations
Respiratory, thoracic and mediastinal disorders	Rare Unknown	nasal discomfort, pharyngolaryngeal pain, sensation of foreign body (throat) dyspnoea
Gastrointestional disorders	Uncommon Rare Not known	dysgeusia vomiting nausea
Hepatobiliary disorders	Rare	alanine aminotransferase increased, gamma-glutamyl transferase increased
Skin and subcutaneous tissue disorders	Not known	erythema, rash, pruritus, urticaria

Description of selected adverse reactions

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following first dose, have been reported in patients receiving systemic quinolone therapy. Some reactions were accompanied by cardiovascular collapse, loss of consciousness, angioedema (including laryngeal, pharyngeal or facial oedema), airway obstruction, dyspnoea, urticarial and itching.

Ruptures of the shoulder, hand, Achilles, or other tendons that required surgical repair or resulted in prolonged disability have been reported in patients receiving systemic fluoroquinolones. Studies and post marketing experience with systemic quinolones indicate that a risk of these ruptures may be increased in patients receiving corticosteroids, especially geriatric patients and in tendons under high stress, including Achilles tendon.

Paediatric population

In clinical trials, Moxifloxacin Hydrochloride Eye Drops has shown to be safe in paediatric patients, including neonates. In patients under 18 years old, the two most frequent adverse reactions were eye irritation and eye pain, both occurring at an incidence rate of 0.9%.

Based on data from clinical trials involving paediatric patients, including neonates, the type and severity of adverse reactions in the paediatric population are similar to those in adults.

4.9 Overdosage:

The limited holding capacity of the conjunctival sac for ophthalmic products practically precludes any overdosing of the medicinal product.

The total amount of moxifloxacin in a single container is too small to induce adverse effects after accidental ingestion.

5. Pharmacological properties

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5.1 Pharmacodynamic Properties:

Pharmacotherapeutic group: Ophthalmologicals; anti-infectives, other anti-infectives, ATC code: S01A E07.

Mechanism of Action

Moxifloxacin, a fourth-generation fluoroquinolone, inhibits the DNA gyrase and topoisomerase IV required for bacterial DNA replication, repair, and recombination.

Resistance:

Resistance to fluoroquinolones, including moxifloxacin generally occurs by chromosomal mutations in genes encoding DNA gyrase and topoisomerase IV. In Gram-negative bacteria, moxifloxacin resistance can be due to mutations in mar (multiple antibiotic resistance) and the qnr (quinolone resistance) gene systems. Resistance is also associated withexpression of bacteria efflux proteins and inactivating enzymes. Cross-resistance with beta-lactams, macrolides andaminoglycosides is not expected due to differences in mode of action.

Susceptibility Testing Breakpoints

There are no pharmacological data correlated with clinical outcome for moxifloxacin administered as a topical agent. Asa result, the European Committee on Antimicrobial Susceptibility Testing (EUCAST) suggests the following epidemiological cut-off values (ECOFF mg/l) derived from MIC distribution curves to indicate susceptibility to topical moxifloxacin:

Corynebacterium	ND
Staphylococcus aureus	0.25 mg/l
Staphylococcus , coag-neg.	0.25 mg/l
Streptococcus pneumoniae	0.5 mg/l
Streptococcus pyogenes	0.5 mg/l
Streptococcus, viridans group	0.5 mg/l
Enterobacter spp.	0.25 mg/l
Haemophilus influenzae	0.125 mg/l
Klebsiella spp.	0.25 mg/l
Moraxella catarrhalis	0.25 mg/l
Morganella morganii	0.25 mg/l
Neisseria gonorrhoeae	0.032 mg/l
Pseudomonas aeruginosa	4 mg/l
Serratia Marcescens	1 mg/l

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of moxifloxacin in at least some types of infections is questionable.

COMMONLY SUSCEPTIBLE SPECIES
Aerobic Gram-positive micro-organisms: Corynebacterium species including

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Corynebacterium diphtheriae
Staphylococcus aureus (methicillin susceptible)
Streptococcus pneumoniae
Streptococcus pyogenes
Streptococcus viridans Group

Aerobic Gram-negative micro-organisms:
Enterobacter cloacae
Haemophilus influenzae
Klebsiella oxytoca
Moraxella catarrhalis
Serratia marcescens

Anaerobic micro-organisms:
Proprionibacterium acnes

Other micro-organisms:
Chlamydia trachomatis

SPECIES FOR WHICH ACQUIRED RESISTANCE MAY BE A PROBLEM
Aerobic Gram-positive micro-organisms: Staphylococcus aureus (methicillin resistant) Staphylococcus, coagulase-negative species (methicillin resistant) **Aerobic Gram-negative micro-organisms:** Neisseria gonorrhoeae **Other micro-organisms:** None

INHERENTLY RESISTANT ORGANISMS
Aerobic Gram-negative micro-organisms : Pseudomonas aeruginosa **Other micro-organisms:** None

5.2 Pharmacokinetics Properties:

Plasma concentrations of moxifloxacin were measured in healthy adult male and female subjects who received bilateral topical ocular doses of Moxifloxacin 3 times a day. The mean steady-state C_{max} (2.7 ng/mL) and estimated daily exposure $AUC_{0-\infty}$ (45 ng•hr/mL) values were 1,600 and 1,000 times lower than the mean C_{max} and AUC reported after therapeutic 400 mg doses of moxifloxacin. The plasma half-life of moxifloxacin was estimated to be 13 hours.

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Microbiology

The antibacterial action of moxifloxacin results from inhibition of the topoisomerase II (DNA gyrase) and topoisomerase IV. DNA gyrase is an essential enzyme that is involved in the replication, transcription and repair of bacterial DNA. Topoisomerase IV is an enzyme known to play a key role in the partitioning of the chromosomal DNA during bacterial cell division.

The mechanism of action for quinolones, including moxifloxacin, is different from that of macrolides, aminoglycosides, or tetracyclines. Therefore, moxifloxacin may be active against pathogens that are resistant to these antibiotics and these antibiotics may be active against pathogens that are resistant to moxifloxacin. There is no cross-resistance between moxifloxacin and the aforementioned classes of antibiotics. Cross resistance has been observed between systemic moxifloxacin and some other quinolones.

In vitro resistance to moxifloxacin develops via multiple-step mutations. Resistance to moxifloxacin occurs in vitro at a general frequency of between 1.8×10^{-9} to less than 1×10^{-11} for Gram-positive bacteria.

Moxifloxacin has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections as described in the INDICATIONS AND USAGE section:

Aerobic Gram-positive microorganisms:

Listeria monocytogenes, Staphylococcus saprophyticus, Streptococcus agalactiae, Streptococcus mitis, Streptococcus pyogenes, Streptococcus Group C, G and F

Aerobic Gram-negative microorganisms:

Acinetobacter baumannii, Acinetobacter calcoaceticus, Citrobacter freundii, Citrobacter koseri, Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumonia, Moraxella catarrhalis, Morganella morganii, Neisseria gonorrhoeae, Proteus mirabilis, Proteus vulgaris, Pseudomonas stutzeri

Aerobic Microorganism :

Clostridium perfringens, Fusobacterium species, Prevotella species, Propionibacterium acnes,

Other microorganisms:

Chlamydia pneumonia, Legionella pneumophila, Mycobacterium avium, Mycobacterium marinum, Mycoplasma pneumoniae

5.3 Preclinical Safety data:

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis:

Long-term studies in animals to determine the carcinogenic potential of moxifloxacin have not been performed. However, in an accelerated study with initiators and promoters, moxifloxacin was not carcinogenic in rats following up to 38 weeks of oral dosing at 500 mg/kg/day (3224 times the highest recommended total daily human ophthalmic dose for a 60 kg person, based on body surface area).

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	Mutagenesis: Moxifloxacin was not mutagenic in four bacterial strains used in the Ames Salmonella reversion assay. As with other quinolones, the positive response observed with moxifloxacin in strain TA 102 using the same assay may be due to the inhibition of DNA gyrase. Moxifloxacin was not mutagenic in the CHO/HGPRT mammalian cell gene mutation assay. An equivocal result was obtained in the same assay when v79 cells were used. Moxifloxacin was clastogenic in the v79 chromosome aberration assay, but it did not induce unscheduled DNA synthesis in cultured rat hepatocytes. There was no evidence of genotoxicity in vivo in a micronucleus test or a dominant lethal test in mice. **Impairment of Fertility:** Moxifloxacin had no effect on fertility in male and female rats at oral doses as high as 500 mg/kg/day, approximately 3224 highest recommended total daily human ophthalmic dose, based on body surface area. At 500 mg/kg orally there were slight effects on sperm morphology (head-tail separation) in male rats and on the estrous cycle in female rats.
6.	**Pharmaceutical particulars**
	6.1 List of Excipients: Boric acid, Borax, Sodium Chloride, Water for Injection
	6.2 Incompatibilities: Not applicable
	6.3 Shelf life: 3 Years (Unopened), One month after first opening.
	6.4 Special Precautions for storage: Do not store above 30ºC. Protect from direct sunlight
	6.5 Nature and contents of container: Opaque low-density polyethylene of 5 ml or 3ml bottle with open translucent open nozzle, plastic closure and HDPE cap packed in carton along with pack insert.
7.	**Marketing Authorization Holder:** Manufacturing Site : Ajanta Pharma Ltd. Mirza - Palashbhari Road, Village Kokhjar, Kamrup (R), Guwahati, Assam – 781128 Registered office: Ajanta House, Charkop, Kandiali (W), Mumbai 400 067 India.
	Marketing Authorization Numbers: Not Applicable
8.	**Date of first authorization/ renewal of the authorization:** Not Applicable
9.	**Date of revision of text:** May 2023

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