## The summary of product characteristics

-Attached

## 1. NAME OF THE MEDICINAL PRODUCT

**OPTALYN**
(Olopatadine Hydrochloride Ophthalmic Solution USP 0.2%)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**Qualitative Declaration:**

**Olopatadine Hydrochloride Ophthalmic Solution USP 0.2%**

- **Olopatadine Hydrochloride**

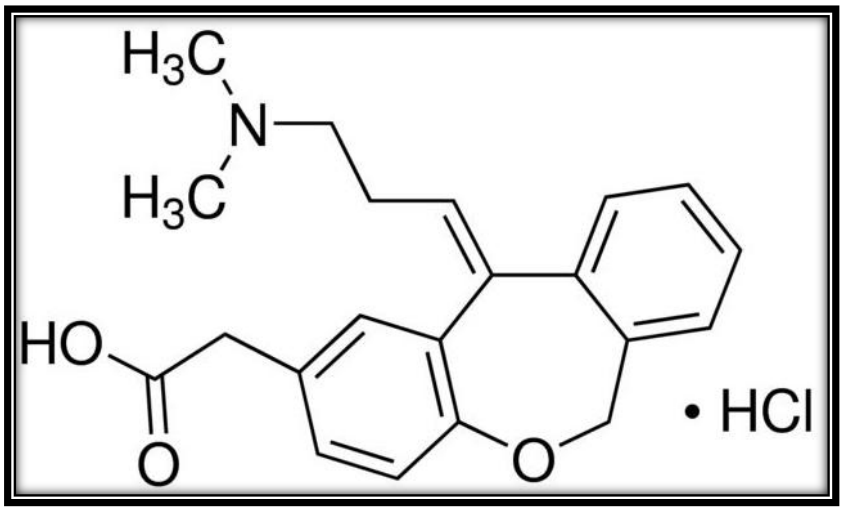
**Chemical Name:**

{(11*Z*)-11-[3-(dimethylamino) propylidene]-6, 11-dihydrodibenzo [*b*,*e*]oxepin-2-yl}acetic acid

**Molecular Weight: -** 373.877 g/mol

**Molecular Formula: -** $C_{21}H_{24}ClNO_3$

**Structural Formula:-**




**Pharmaceutical Form Visual description of the appearance of product:**

Clear Colourless to slightly yellow colour solution, free from any type of visible particles.

**Quantitative Declaration:**

**Composition:**

| | | |
|---|---|---|
| Olopatadine Hydrochloride | USP | |
| Eq. to Olopatadine | | 0.2% w/v |
| Benzalkonium Chloride Solution (As Preservative) | NF | 0.01% w/v |
| Sterile aqueous base | | Q.S |

## 3. PHARMACEUTICAL FORM

Eye Drops

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

**INDICATIONS AND USAGE**

Olopatadine hydrochloride ophthalmic solution 0.2% is indicated for the treatment of the signs and symptoms of allergic conjunctivitis.

## 4.2 Posology and method of administration

## DOSAGE AND ADMINISTRATION

The recommended dose is one drop in each affected eye Once or Twice a day as directed by the Prescriber.

### 4.3 Contraindications

**Contraindications**
Hypersensitivity to the active substance or to any of the excipients

**4.4 Special warnings and precautions for use**

**Warnings and Precautions**

It is an antiallergic/antihistaminic agent and, although administered topically, is absorbed systemically. If signs of serious reactions or hypersensitivity occur, discontinue the use of this treatment.

It contains Benzalkonium chloride which may cause eye irritation.

Benzalkonium chloride has also been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. Close monitoring is required with frequent or prolonged use in dry eye patients, or in conditions where the cornea is compromised.

*Contact lenses*

Benzalkonium is known to discolour soft contact lenses. Avoid contact with soft contact lenses. Patients should be instructed to remove contact lenses prior to administration of the eye drop and wait at least15 minutes after instillation before re-inserting contact lenses.

### 4.5 Interaction with other medicinal products and other forms of interaction

**Drug Interactions**

No interaction studies with other medicinal products have been performed.
*In vitro* studies have shown that olopatadine did not inhibit metabolic reactions which involve cytochrome P-450 isozymes 1A2, 2C8, 2C9, 2C19, 2D6, 2E1 and 3A4. These results indicate that olopatadine is unlikely to result in metabolic interactions with other concomitantly administered active substances.

**4.6 Fertility, pregnancy and lactation**

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**
There are no or limited amount of data from the use of ophthalmic Olopatadine in pregnant women.
Studies in animals have shown reproductive toxicity following systemic administration.
Olopatadine is not recommended during pregnancy and in women of childbearing potential not using contraception.

**Lactation**
Available data in animals have shown excretion of Olopatadine in milk following oral administration.
A risk to the newborn/infants cannot be excluded.
It should not be used during breast-feeding.

**Fertility**
Studies have not been performed to evaluate the effect of topical ocular administration of Olopatadine on human fertility.

**4.7 Effects on ability to drive and use machines**

It has no or negligible influence on the ability to drive and use machines.
As with any eye drop, temporary blurred vision or other visual disturbances may affect the ability to drive or use machines. If blurred vision occurs at instillation, the patient must wait until the vision clears before driving or using machinery.

### 4.8 Undesirable effects

The following adverse reactions have been reported during clinical studies and post-marketing data 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 <1/1000) 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.

| **System Organ Classification** | **Frequency** | **Adverse Reactions** |
|---|---|---|
| Infections and infestations | Uncommon | rhinitis |
| Immune system disorders | Not known | hypersensitivity, swelling face |
| Nervous system disorders | Common | headache, dysgeusia |
| | Uncommon | dizziness, hypoaesthesia |
| | Not known | somnolence |
| Eye disorders | Common | eye pain, eye irritation, dry eye, abnormal sensation in eyes |
| | Uncommon | corneal erosion, corneal epithelium defect, corneal epithelium disorder, punctate keratitis, keratitis, corneal staining, eye discharge, photophobia, vision blurred, visual acuity reduced, blepharospasm, ocular discomfort, eye pruritus, conjunctival follicles, conjunctival disorder, foreign body sensation in eyes, lacrimation increased, erythema of eyelid, eyelid oedema, eyelid disorder, ocular hyperaemia |
| | Not known | corneal oedema, eye oedema, eye swelling, conjunctivitis, mydriasis, visual disturbance, eyelid margin crusting |
| Respiratory, thoracic, and mediastinal disorders | Common | nasal dryness |
| | Not known | dyspnoea, sinusitis |
| Gastrointestinal disorders | Not known | nausea, vomiting |

| | | |
|---|---|---|
| Skin and subcutaneous tissue disorders | Uncommon | dermatitis contact, skin burning sensation, dry skin |
| | Not known | dermatitis, erythema |
| General disorders and administration site conditions | Common | fatigue |
| | Not known | asthenia, malaise |

Cases of corneal calcification have been reported very rarely in association with the use of phosphate containing eye drops in some patients with significantly damaged corneas.

**4.9 Overdose**

**OVERDOSAGE**

No data are available in humans regarding overdose by accidental or deliberate ingestion. Olopatadine has a low order of acute toxicity in animals. Accidental ingestion of the entire contents of a bottle of olopatadine would deliver a maximum systemic exposure of 5 mg olopatadine. This exposure would result in a final dose of 0.5 mg/kg in a 10 kg infant, assuming 100% absorption.

Prolongation of the QTc interval in dogs was observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use. A 5 mg oral dose was administered twice-daily for 2.5 days to 102 young and elderly male and female healthy volunteers with no significant prolongation of QTc interval compared to placebo. The range of peak steady-state olopatadine plasma concentrations (35 to 127 ng/ml) seen in this study represents at least a 70-fold safety margin for topical olopatadine with respect to effects on cardiac repolarization.

In the case of overdose, appropriate monitoring and management of the patient should be implemented.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamics properties

**Pharmacodynamics properties:**

Pharmacotherapeutic group: Anticholinergic
ATC code: S01GX09

**Pharmacodynamics properties:**
Used to treat allergic conjunctivitis (itching eyes), Olopatadine inhibits the release of histamine from mast cells. It is a relatively selective histamine H1 antagonist that inhibits the in vivo and in vitro type 1 immediate hypersensitivity reaction including inhibition of histamine induced effects on human conjunctival epithelial cells.

Olopatadine is a potent selective antiallergic/antihistaminic agent that exerts its effects through multiple distinct mechanisms of action. It antagonises histamine (the primary mediator of allergic response in humans) and prevents histamine induced inflammatory cytokine production by human conjunctival epithelial cells. Data from in vitro studies suggest that it may act on human conjunctival mast cells to inhibit the release of pro-inflammatory mediators also invivodata suggest that it inhibits type 1 hypersensitivity reaction. In patients with patent nasolacrimal ducts, topical ocular administration of Olopatadine hydrochloride ophthalmic solution 0.2% was suggested to reduce the nasal signs and symptoms that frequently accompany seasonal allergic conjunctivitis. It does not produce a clinically significant change in pupil diameter. Olopatadine is devoid of effects on alphaadrenergic, dopamine, and muscarinic type 1 and 2 receptors.

**Mechanism of action:**
Olopatadine is a selective histamine H1 antagonist that binds to the histamine H1 receptor. This blocks the action of endogenous histamine, which subsequently leads to temporary relief of the negative symptoms brought on by histamine. Olopatadine is devoid of effects on alpha-adrenergic, dopamine and muscarinic type 1 and 2 receptors.

Olopatadine is a mast cell stabilizer and a histamine H1 antagonist. Decreased chemotaxis and inhibition of eosinophil activation has also been demonstrated.

**Application:**
Olopatadine is an antihistamine that reduces the natural chemical histamine in the body. Histamine can produce symptoms of itching or watery eyes. Olopatadine ophthalmic is used to treat ocular (eye) symptoms of allergic conditions, such as inflammation, itching, watering, and burning.

Olopatadine is a potent selective Antiallergics/antihistaminic agent that exerts its effects through multiple distinct mechanisms of action. It antagonises histamine (the primary mediator of allergic response in humans) and prevents histamine induced inflammatory cytokine production by human conjunctival epithelial cells. Data from in vitro studies suggest that it may act on human conjunctival mast cells to inhibit the release of pro-inflammatory mediators. In patients with patent nasolacrimal ducts, topical ocular administration of Olopatadine was suggested to reduce the nasal signs and symptoms that frequently accompany seasonal allergic conjunctivitis. It does not produce a clinically significant change in pupil diameter.

**5.2 Pharmacokinetics Properties**

**Pharmacokinetics**

**Absorption**
Olopatadine is absorbed systemically, as are other topically administered medicinal products. However, systemic absorption of topically applied olopatadine is minimal with plasma concentrations ranging from below the assay quantitation limit (<0.5 ng/ml) up to 1.3 ng/ml. These concentrations are 50-to 200-fold lower than those following well tolerated oral doses.

**Elimination**
From oral pharmacokinetic studies, the half-life of olopatadine in plasma was approximately eight to 12 hours, and elimination was predominantly through renal excretion. Approximately 60-70% of the dose was recovered in the urine as active substance. Two metabolites, the mono-desmethyl and the N-oxide, were detected at low concentrations in the urine.

Since olopatadine is excreted in urine primarily as unchanged active substance, impairment of renal function alters the pharmacokinetics of olopatadine with peak plasma concentrations 2.3-fold greater in patients with severe renal impairment (mean creatinine clearance of 13.0 ml/min) compared to healthy adults. Following a 10 mg oral dose in patients undergoing haemodialysis (with no urinary output), plasma olopatadine concentrations were significantly lower on the haemodialysis day than on the non-haemodialysis day suggesting olopatadine can be removed by hemodialysis.

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

Olopatadine administered orally was not carcinogenic in mice and rats in doses up to 500 mg/kg/day and 200 mg/kg/day, respectively. Based on a 40 µL drop size and a 50 kg person, these doses were approximately 150,000 and 50,000 times higher than the maximum recommended ocular human dose (MROHD). No mutagenic potential was observed when Olopatadine was tested in an in vitro bacterial reverse mutation (Ames) test, an in vitro mammalian chromosome aberration assay or an in vivo mouse micronucleus test. Olopatadine administered to male and female rats at oral doses of approximately 100,000 times MROHD level resulted in a slight decrease in the fertility index and reduced implantation rate; no effects on reproductive function were observed at doses of approximately 15,000 times the MROHD level.

**5.3 Preclinical safety data**

**Clinical Studies**

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

Studies in animals have shown reduced growth of nursing pups of dams receiving systemic doses of Olopatadine well in excess of the maximum level recommended for human ocular use. Olopatadine has been detected in the milk of nursing rats following oral administration.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

| | |
|---|---|
| BENZALKONIUM CHLORIDE SOLUTION | NF |
| EDETATE DISODIUM | NF |
| SODIUM CHLORIDE | BP/USP/NF |
| SODIUM DIHYDROGEN PHOSPHATE | BP |
| ANHYDROUS DISODIUM HYDROGEN PHOSPHATE | BP |
| SODIUM HYDROXIDE PELLETS | NF |
| PURIFIED WATER | BP/IH |

## 6.2Incompatibilities

Not applicable.

**6.3 Shelf life**

24 months

**Use the solution within one month after opening the container.**

### 6.4 Special precautions for storage

Store below 30ºC. Do not freeze.

Protect from light.

Keep out of the reach of children.

Prescription only Medicine.

**6.5 Nature and contents of container**

The **Olopatadine Hydrochloride Ophthalmic Solution USP** packed in 5ml sterile **opaque plastic bottle with nozzle & cap**. Each bottle is packed in monocarton with pack inset inside the carton. Such Packed cartons are shrinked with shrink bags in quantity of 25 nos.

5 ml Olopatadine Hydrochloride Ophthalmic Solution USP is packed in 5 ml three piece white color opaque plastic bottle containing low density polyethylene (LDPE) white color opaque bottle, low density polyethylene (LDPE) white color opaque nozzle / dropper and high density polyethylene (HDPE) white color opaque ca with pilfer proof seal.

The liquid is filled in a multi dose container, and contain Benzalkonium Chloride Solution, Edetate Disodium, Sodium Chloride, Sodium Dihydrogen Phosphate, Anhydrous Disodium Hydrogen Phosphate, and Sodium Hydroxide Pellets for pH adjustment.

**6.6 Special precaution for disposal of a used medicinal product or waste materials derived such medicinal product and other handling of the product**

No special requirements

## 7. Marketing Authorization Holder

**Brand Owner & Marketing Authorisation Holder**
Korlyns Therapeutics Ltd.
Linkfield Lane, Redhill, Surrey,
England, UK.

## Applicant

**KORLYNS PHARMACEUTICALS LTD.**
No 31B, AdeyemiAdeoye Street,
Off AdeyemiAdeoye Road,
Opposite Health Centre, Wasimi,
Maryland, Lagos.
Telephone: 09064597759

**Manufactured By:**
**INDIANA OPHTHALMICS LLP**

132,135,136,137, G.I.D.C ESTATE,

WADHWAN CITY – 363035,

DIST.: SURENDRANAGAR,

GUJARAT, INDIA.

**8. Number in the national register of finished pharmaceutical products**

~Not Applicable~

**9. Date of first authorization/renewal of the authorization**

~Not Applicable~

**10. Date of revision of the text**

16/10/2015