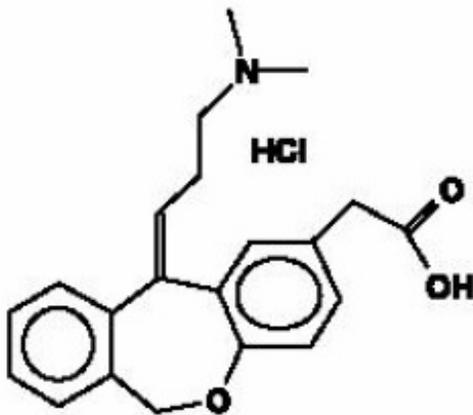


**OLOPATADINE HYDROCHLORIDE - olopatadine hydrochloride solution/ drops**  
**Alembic Pharmaceuticals Inc.**

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**OLOPATADINE HYDROCHLORIDE ophthalmic solution**  
**Initial U.S. Approval: 1996**

**DESCRIPTION**

Olopatadine hydrochloride ophthalmic solution USP, 0.1% is a sterile ophthalmic solution containing olopatadine, a relatively selective H<sub>1</sub>-receptor antagonist and inhibitor of histamine release from the mast cell for topical administration to the eyes. Olopatadine hydrochloride, USP is a white, crystalline, water-soluble powder with a molecular weight of 373.88. The chemical structure is presented below:



**Chemical Name:** 11-[(Z)-3-(Dimethylamino)propylidene]-6-11-dihydrodibenz[b,e]oxepin-2-acetic acid hydrochloride

Each mL of olopatadine hydrochloride ophthalmic solution USP, 0.1 % contains: **Active:** 1.11 mg olopatadine hydrochloride, USP equivalent to 1 mg olopatadine.

Preservative: Benzalkonium chloride 0.01%. Inactives: Dibasic sodium phosphate; Sodium chloride; Hydrochloric acid/Sodium hydroxide (adjust pH); and Water for Injection. It has a pH of approximately 7 and an osmolality of approximately 300 mOsm/kg.

**CLINICAL PHARMACOLOGY**

Olopatadine is an inhibitor of the release of histamine from the mast cell and a relatively selective histamine H<sub>1</sub>-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 devoid of effects on alpha-adrenergic, dopamine and muscarinic type 1 and 2 receptors. Following topical ocular administration in man, olopatadine was shown to have low systemic exposure. Two studies in normal volunteers (totaling 24 subjects) dosed bilaterally with olopatadine 0.15% ophthalmic solution once every 12 hours for 2 weeks demonstrated plasma concentrations to be generally below the quantitation limit of the assay (<0.5 ng/mL). Samples in which olopatadine was quantifiable were typically found within 2 hours of dosing and ranged from 0.5 to 1.3 ng/mL. The half-life in plasma was

approximately 3 hours, and elimination was predominantly through renal excretion. Approximately 60-70% of the dose was recovered in the urine as parent drug. Two metabolites, the mono-desmethyl and the N-oxide, were detected at low concentrations in the urine.

Results from an environmental study demonstrated that olopatadine hydrochloride ophthalmic solution USP, 0.1% was effective in the treatment of the signs and symptoms of allergic conjunctivitis when dosed twice daily for up to 6 weeks. Results from conjunctival antigen challenge studies demonstrated that Olopatadine hydrochloride ophthalmic solution USP, 0.1% when subjects were challenged with antigen both initially and up to 8 hours after dosing, was significantly more effective than its vehicle in preventing ocular itching associated with allergic conjunctivitis.

## **INDICATIONS AND USAGE**

Olopatadine hydrochloride ophthalmic solution USP, 0.1% is indicated for the treatment of the signs and symptoms of allergic conjunctivitis.

## **CONTRAINDICATIONS**

Olopatadine hydrochloride ophthalmic solution USP, 0.1% is contraindicated in persons with a known hypersensitivity to olopatadine hydrochloride, USP or any components of olopatadine hydrochloride ophthalmic solution USP, 0.1%.

## **WARNINGS**

Olopatadine hydrochloride ophthalmic solution USP, 0.1% is for topical use only and not for injection or oral use.

## **PRECAUTIONS**

### **INFORMATION FOR PATIENTS**

To prevent contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use. Patients should be advised not to wear a contact lens if their eye is red. Olopatadine hydrochloride ophthalmic solution USP, 0.1% should not be used to treat contact lens related irritation. The preservative in Olopatadine hydrochloride ophthalmic solution USP, 0.1%, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses and **whose eyes are not red** should be instructed to wait at least ten minutes after instilling Olopatadine hydrochloride ophthalmic solution USP, 0.1% before they insert their contact lenses.

### **CARCINOGENESIS AND MUTAGENESIS AND 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, these doses were 78,125 and 31,250 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 62,500 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 7,800 times the maximum recommended ocular human use level.

### **PREGNANCY**

**Pregnancy Category C.** Olopatadine was found not to be teratogenic in rats and rabbits. However, rats treated at 600 mg/kg/day, or 93,750 times the MROHD and rabbits treated at 400 mg/kg/day, or 62,500

times the MROHD, during organogenesis showed a decrease in live fetuses. There are, however, no adequate and well controlled studies in pregnant women. Because animal studies are not always predictive of human responses, this drug should be used in pregnant women only if the potential benefit to the mother justifies the potential risk to the embryo or fetus.

### **NURSING MOTHERS**

Olopatadine has been identified in the milk of nursing rats following oral administration. It is not known whether topical ocular administration could result in sufficient systemic absorption to produce detectable quantities in the human breast milk. Nevertheless, caution should be exercised when Olopatadine hydrochloride ophthalmic solution USP, 0.1% is administered to a nursing mother.

### **PEDIATRIC USE**

Safety and effectiveness in pediatric patients below the age of 3 years have not been established.

### **GERIATRIC USE**

No overall differences in safety or effectiveness have been observed between elderly and younger patients.

### **ADVERSE REACTIONS**

Headaches have been reported at an incidence of 7%. The following adverse experiences have been reported in less than 5% of patients: Asthenia, blurred vision, burning or stinging, cold syndrome, dry eye, foreign body sensation, hyperemia, hypersensitivity, keratitis, lid edema, nausea, pharyngitis, pruritis, rhinitis, sinusitis, and taste perversion. Some of these events were similar to the underlying disease being studied.

### **DOSAGE AND ADMINISTRATION**

The recommended dose is one drop in each affected eye two times per day at an interval of 6 to 8 hours.

### **HOW SUPPLIED**

Olopatadine hydrochloride ophthalmic solution USP, 0.1% is supplied as follows: 5 mL in 5 mL screw neck white low density polyethylene bottle.  
5 mL: NDC 62332-501-05

**Storage:** Store at 4° to 25°C (39° to 77°F)

### **Rx Only**

#### **Manufactured for:**

Alembic Pharmaceuticals, Inc.  
750 Route 202, Bridgewater, NJ 08807  
USA

#### **Manufactured by:**

Gland Pharma Limited  
D.P. Pally, Dundigal Post,  
Hyderabad-500 043, India

Revised: 12/2018

**PACKAGE LABEL.PRINCIPAL DISPLAY PANEL**

NDC 62332-501-05  
Olopatadine Hydrochloride Ophthalmic Solution USP, 0.1%  
Rx only  
5 ml  
Sterile  
Almebic

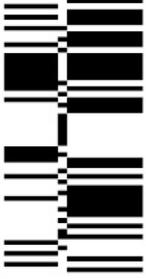
**Rx only** **5 mL**  
**\*Each mL contains:** Olopatadine 1 mg  
**USUAL DOSAGE:** Read enclosed insert.  
**STORAGE:** Store at 4°C to 25°C (39°F to 77°F).  
Manufactured for:  
**Alembic Pharmaceuticals, Inc.**  
750 Route 202, Bridgewater, NJ 08807  
USA  
Made in India.

**NDC 62332-501-05**  
**Olopatadine Hydrochloride**  
**Ophthalmic Solution**  
**USP, 0.1%\***

FOR USE IN THE EYES ONLY



LAB-020314-00 12/2018  
M.L.No.: 103/AP/RR/97/F/R



(01)0 0362332-501-05 2

LOT:  
EXP:

NDC 62332-501-05  
Olopatadine Hydrochloride Ophthalmic Solution USP, 0.1%  
Rx only  
5 ml  
Sterile  
Almebic



## OLOPATADINE HYDROCHLORIDE

olopatadine hydrochloride solution/ drops

### Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:62332-501
Route of Administration	OPHTHALMIC		

**Active Ingredient/Active Moiety**

Ingredient Name	Basis of Strength	Strength
<b>OLOPATADINE HYDROCHLORIDE</b> (UNII: 2XG66W44KF) (OLOPATADINE - UNII:D27V6190PM)	OLOPATADINE	1 mg in 1 mL

### Inactive Ingredients

Ingredient Name	Strength
<b>SODIUM PHOSPHATE, DIBASIC, UNSPECIFIED FORM</b> (UNII: GR686LBA74)	
<b>SODIUM CHLORIDE</b> (UNII: 451W47IQ8X)	
<b>HYDROCHLORIC ACID</b> (UNII: QTT17582CB)	
<b>SODIUM HYDROXIDE</b> (UNII: 55X04QC32I)	
<b>WATER</b> (UNII: 059QF0K00R)	
<b>BENZALKONIUM CHLORIDE</b> (UNII: F5UM2KM3W7)	

### Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:62332-501-05	1 in 1 CARTON	12/07/2018	
1		5 mL in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product		

### Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA209919	12/07/2018	

**Labeler** - Alembic Pharmaceuticals Inc. (079288842)

### Establishment

Name	Address	ID/FEI	Business Operations
Gland Pharma Limited		918601238	MANUFACTURE(62332-501)

Revised: 2/2019

Alembic Pharmaceuticals Inc.