LIVOSTIN- levocabastine hydrochloride suspension
Novartis Ophthalmics

Livostin®

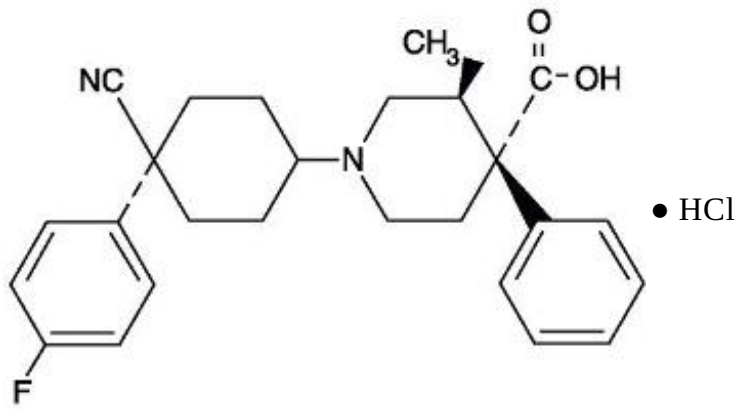
LIVOSTIN®

0.05% (levocabastine hydrochloride ophthalmic suspension)

DESCRIPTION

LIVOSTIN™ 0.05% (levocabastine hydrochloride ophthalmic suspension) is a selective histamine H_1-receptor antagonist for topical ophthalmic use. Each mL contains 0.54 mg levocabastine hydrochloride equivalent to 0.5 mg levocabastine; 0.15 mg benzalkonium chloride; propylene glycol; polysorbate 80; dibasic sodium phosphate, anhydrous; monobasic sodium phosphate, monohydrate; disodium edetate; hydroxypropyl methylcellulose; and purified water. It has a pH of 6.0 to 8.0.

The chemical name for levocabastine hydrochloride is (–)-*trans*-1-[*cis*-4-Cyano-4- (p-fluorophenyl)cyclohexyl]-3-methyl-4-phenylisonipecotic acid monohydrochloride, and is represented by the following chemical structure:



CLINICAL PHARMACOLOGY

Levocabastine is a potent, selective histamine H_1-antagonist.

Antigen challenge studies performed two and four hours after initial drug instillation indicated activity was maintained for at least two hours.

In an environmental study, LIVOSTIN™ 0.05% (levocabastine hydrochloride ophthalmic suspension) instilled four times daily was shown to be significantly more effective than its vehicle in reducing ocular itching associated with seasonal allergic conjunctivitis.

After instillation in the eye, levocabastine is systemically absorbed. However, the amount of systemically absorbed levocabastine after therapeutic ocular doses is low (mean plasma concentrations in the range of 1-2 ng/mL).

INDICATIONS AND USAGE

LIVOSTIN™ 0.05% (levocabastine hydrochloride ophthalmic suspension) is indicated for the temporary relief of the signs and symptoms of seasonal allergic conjunctivitis.

CONTRAINDICATIONS

This product is contraindicated in persons with known or suspected hypersensitivity to any of its components. It should not be used while soft contact lenses are being worn.

WARNING

For topical use only. Not for injection.

PRECAUTIONS

Information for Patients

SHAKE WELL BEFORE USING. To prevent contaminating the dropper tip and suspension, 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. Do not use if the suspension has discolored. Store at controlled room temperature. Protect from freezing.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Levocabastine was not carcinogenic in male or female rats or in male mice when administered in the diet for up to 24 months. In female mice, levocabastine doses of 5,000 and 21,500 times the maximum recommended ocular human use level resulted in an increased incidence of pituitary gland adenoma and mammary gland adenocarcinoma possibly produced by increased prolactin levels. The clinical relevance of this finding is unknown with regard to the interspecies differences in prolactin physiology and the very low plasma concentrations of levocabastine following ocular administration.

Mutagenic potential was not demonstrated for levocabastine when tested in Ames' Salmonella reversion test or in *Escherichia coli, Drosophila melanogaster,* a mouse Dominant Lethal Assay or in rat Micronucleus test.

In reproduction studies in rats, levocabastine showed no effects on fertility at oral doses of 20 mg/kg/day (8,300 times the maximum recommended human ocular dose).

PREGNANCY

Teratogenic Effects

Pregnancy Category C.

Levocabastine has been shown to be teratogenic (polydactyly) in rats when given in doses 16,500 times the maximum recommended human ocular dose. Teratogenicity (polydactyly, hydrocephaly,

brachygnathia), embryotoxicity, and maternal toxicity were observed in rats at 66,000 times the maximum recommended ocular human dose. There are no adequate and well-controlled studies in pregnant women. Levocabastine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

Based on determinations of levocabastine in breast milk after ophthalmic administration of the drug to one nursing woman, it was calculated that the daily dose of levocabastine in the infant was about 0.5 µg.

Pediatric Use

Safety and effectiveness in pediatric patients below the age of 12 have not been established.

ADVERSE REACTIONS

The most frequent adverse experiences reported with the use of LIVOSTIN™ 0.05% (levocabastine hydrochloride ophthalmic suspension) were mild, transient stinging and burning (29%) and headache (5%).

Other adverse experiences reported in approximately 1-3% of patients treated with LIVOSTIN™ were visual disturbances, dry mouth, fatigue, pharyngitis, eye pain/dryness, somnolence, red eyes, lacrimation/discharge, cough, nausea, rash/erythema, eyelid edema, and dyspnea.

DOSAGE AND ADMINISTRATION

SHAKE WELL BEFORE USING. The usual dose is one drop instilled in affected eyes four times per day.

HOW SUPPLIED

LIVOSTIN™ 0.05% (levocabastine hydrochloride ophthalmic suspension), 2.5 mL, 5 mL, and 10 mL is provided in white, polyethylene dropper tip squeeze bottles.

Keep tightly closed when not in use.

Do not use if the suspension has discolored.

Store at controlled room temperature 15°to 30°C (59° to 86°F).

Protect from freezing.

NDC 58768-610-10 (10.0 mL)

NDC 58768-610-05 (5.0 mL)

NDC 58768-610-99 (2.5 mL)

Rx Only

Levocabastine hydrochloride is an original product of Janssen Pharmaceutica Inc.

Mfd. by OMJ Pharmaceuticals, Inc.,
San Germán, P.R., 00683 for:
Novartis Ophthalmics, Duluth, GA 30097

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LIVOSTIN

levocabastine hydrochloride suspension

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:58768-610
Route of Administration	OPHTHALMIC		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
levocabastine hydrochloride (UNII: 124XMA6YEI) (levocabastine - UNII:H68BP06S81)		0.5 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
benzalkonium chloride ()	0.15 mg in 1 mL
dibasic sodium phosphate, anhydrous ()	
disodium edetate ()	
hydroxypropyl methylcellulose ()	
monobasic sodium phosphate, monohydrate ()	
polysorbate 80 ()	
propylene glycol (UNII: 6DC9Q167V3)	
water (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:58768-610-05	5 mL in 1 BOTTLE, DROPPER		
2	NDC:58768-610-10	10 mL in 1 BOTTLE, DROPPER		
3	NDC:58768-610-99	2.5 mL in 1 BOTTLE, DROPPER		

Labeler - Novartis Ophthalmics