PRODUCT MONOGRAPH

[Pr] MINT-OLOPATADINE

Olopatadine Hydrochloride Ophthalmic Solution
0.1% w/v (as olopatadine hydrochloride)

USP

Anti-allergy Agent

Mint Pharmaceuticals Inc.
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Mississauga, Ontario
Canada L5T 2M3

Date of Revision:
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Control Number:

241215

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[Pr]MINT-OLOPATADINE
Olopatadine Hydrochloride Ophthalmic Solution
0.1% w/v (as olopatadine hydrochloride)

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	All Nonmedicinal Ingredients
Topical Ophthalmic	Ophthalmic Solution/0.1% w/v olopatadine (as olopatadine hydrochloride)	Preservative: benzalkonium chloride Non-medicinal ingredients: dibasic sodium phosphate dodecahydrate, hydrochloric acid and/or sodium hydroxide (to adjust pH), purified water, sodium chloride

INDICATIONS AND CLINICAL USE

MINT-OLOPATADINE (olopatadine hydrochloride) ophthalmic solution is indicated for the treatment of allergic conjunctivitis.

Geriatrics: No overall difference in safety has been observed between elderly and other adult patients.

Pediatrics (3 – 16 years of age): Olopatadine hydrochloride ophthalmic solution administered three times a day for six weeks was shown to be safe and well-tolerated in subjects who were ages 3 years and older.

CONTRAINDICATIONS

Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see Dosage Forms, Composition and Packaging section of the Product Monograph.

WARNINGS AND PRECAUTIONS

General

For topical ocular use only. Not for injection or oral use.
As with any eye drop, to prevent contamination of 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 contact lenses if their eye(s) are red.

The preservative in MINT-OLOPATADINE, benzalkonium chloride, may cause eye irritation and is known to discolour soft contact lenses. Contact with soft contact lenses should be avoided. Patients must be instructed to remove contact lenses prior to application of MINT-OLOPATADINE and wait at least 15 minutes before they insert their contact lenses.

If using other eye drops, patients should wait at least 5 minutes between putting in MINT-OLOPATADINE and the other drops. Eye ointments should be applied last.

Driving and Using Machinery

Olopatadine is a non-sedating anti-histamine. Temporary blurred vision or other visual disturbances, after the use of MINT-OLOPATADINE, may affect the ability to drive or use machines. If blurred vision occurs after instillation, patients must wait until vision clears before driving or using machinery.

Carcinogenesis and Mutagenesis

Please refer to animal data in TOXICOLOGY section.

Sexual Function/Reproduction

Studies have not been performed to evaluate the effect of topical ocular administration of olopatadine on human fertility. Olopatadine administered to male and female rats at oral doses of 62,500 times the maximum recommended ocular human use 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.

Special Populations

Pregnant Women:

There are no adequate and well controlled studies in pregnant women. Studies in animals with olopatadine have shown reproductive toxicity following systemic administration considered sufficiently in excess of the maximum human exposure. Olopatadine was found not to be teratogenic in rats and rabbits at oral doses >90,000 and >60,000 times the maximum recommended ocular human use level, respectively. 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 Women:

Olopatadine has been identified in the milk of nursing rats following oral administration. Rat pups of mothers administered olopatadine orally at greater than 625 times (but not at 312 times) the maximum recommended ocular human use level demonstrated reduced body weight gain during the nursing period. It is not known whether topical ocular administration could result in sufficient systemic absorption to produce detectable quantities in human breast milk.

Nevertheless, caution should be exercised when MINT-OLOPATADINE is administered to a nursing mother.

Geriatrics: No overall difference in safety has been observed between elderly and other adult patients.

Pediatrics (3 – 16 years of age): The safety and effectiveness of olopatadine hydrochloride ophthalmic solution have been established in pediatric patients between 3 and 16 years of age.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

In clinical studies of olopatadine hydrochloride ophthalmic solution, ocular and non-ocular adverse reactions related to therapy were reported at an incidence below 1%. |

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Less Common Clinical Trial Adverse Drug Reactions

Ocular: ocular discomfort (including mild transient burning or stinging and foreign body sensation), eye pruritis, ocular hyperemia, superficial keratitis, eyelid edema, dry eye, eyelid dryness, eyelid spasm, photophobia

Non-ocular: asthenia, headache, dysgeusia.

Post-Market Adverse Drug Reactions

Approximately 30.5 million units of olopatadine hydrochloride ophthalmic solution have been sold in 69 countries. The reporting rate of all reaction terms reported between 01 January 1997 and 31 December 2004 was 0.004%, and no single reaction term occurred with a reporting rate greater than 0.0007%.

There were no new major findings bearing on the established overall safety profile of olopatadine hydrochloride ophthalmic solution.

Adverse drug reactions identified from post-marketing experience that have not been reported previously in the above-mentioned clinical trials with olopatadine hydrochloride ophthalmic solution include: dizziness, eye pain, eye discharge, eyelid margin crusting, vision blurred, punctate keratitis, keratitis, erythema of eyelid, nasal dryness, dry mouth, dermatitis contact, fatigue, hypersensitivity, lacrimation increased and nausea.

DRUG INTERACTIONS

No clinical interaction studies have been conducted with olopatadine hydrochloride ophthalmic solution. *In vitro* studies have shown that olopatadine does not inhibit metabolic reactions which involve cytochrome P-450 isoenzymes 1A2, 2C8, 2C9, 2C19, 2D6, 2E1 and 3A4. Olopatadine is moderately bound to plasma proteins (approximately 55%).These results indicate that olopatadine is unlikely to result in interactions with other concomitantly administered medications. Due to the low systemic exposure following topical ocular dosing, it is unlikely that olopatadine hydrochloride ophthalmic solution would interfere with immediate hypersensitivity skin testing.

Interactions with other drugs, food, herbal products or laboratory tests have not been established.

DOSAGE AND ADMINISTRATION

Recommended Dose and Dosage Adjustment

The recommended dose is one to two drops in each affected eye twice daily.
No dosage adjustment is required in hepatic or renal impairment.

Missed Dose

If a dose is missed, a single drop should be taken as soon as possible before reverting to regular routine. Do not use a double dose to make up for the one missed.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

A topical overdosage may be flushed from the eye(s) with warm tap water.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Olopatadine, a structural analog of doxepin, is a non-steroidal, non-sedating, topically effective anti-allergic molecule that exerts its effects through multiple distinct mechanisms of action. Olopatadine is a mast cell stabilizer and a potent, selective histamine H_1 antagonist (9, 11) that inhibits the *in vivo* type 1 immediate hypersensitivity reaction (12). Olopatadine inhibits the release of mast cell inflammatory mediators [i.e., histamine, tryptase, prostaglandin D2 and TNFα (4,9,11,12)] as demonstrated in *in vitro* studies and confirmed in patients (7). Olopatadine is also an inhibitor of pro-inflammatory cytokine secretion from human conjunctival epithelial cells (13).

Pharmacodynamics

Effects on cardiac repolarization (QTc):
In two placebo-controlled, two-way crossover cardiac repolarization studies, no signal of QT

interval prolongation was observed relative to placebo following twice daily 5 mg oral doses for 2.5 days in 102 healthy volunteers or following twice daily 20 mg oral doses for 13.5 days in 32 healthy volunteers. In addition, no evidence of QT interval prolongation was observed, relative to placebo, in 429 perennial allergic rhinitis patients given olopatadine hydrochloride nasal spray, 665 micrograms twice daily for up to 1 year.

Pharmacokinetics

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). The half-life in plasma was 7-14 hours, and elimination was predominantly through renal excretion. Approximately 60-70% of the dose was recovered in the urine as parent drug.

Special Populations and Conditions:

Pediatrics: Olopatadine hydrochloride ophthalmic solution administered three times a day for six weeks was shown to be safe and well tolerated in subjects who were 3 years and older.

Geriatrics: No overall differences in safety and effectiveness have been observed between elderly and other adult patients.

Gender: No specific pharmacokinetic study examining the effect of gender was conducted.

Race: No specific pharmacokinetic study examining the effect of race was conducted.

Hepatic Insufficiency: No specific pharmacokinetic study examining the effect of hepatic impairment was conducted. Since metabolism of olopatadine is a minor route of elimination, no adjustment of the dosing regimen of olopatadine hydrochloride ophthalmic solution, 0.1% is warranted in patients with hepatic impairment.

Renal Insufficiency:

The mean plasma C_{max} values for olopatadine following single intranasal doses of olopatadine HCl nasal spray 0.6% (665 µg/spray) were not markedly different between healthy subjects (18.1 ng/mL) and patients with mild, moderate and severe renal impairment (range 15.5 ng/mL to 21.6 ng/mL). Plasma AUC was 2.5-fold higher in patients with severe impairment (creatinine clearance <30 mL/min/1.73m2). Predicted peak steady-state plasma concentrations of olopatadine in patients with renal impairment following administration of olopatadine hydrochloride ophthalmic solution, 0.1% are at least 10-fold lower than those observed following administration of olopatadine nasal spray 0.6%, and approximately 300-fold lower than those observed following the safe and well-tolerated administration of 20 mg oral doses for 13.5 days. These findings indicate that no adjustment of the dosing regimen of olopatadine hydrochloride ophthalmic solution, 0.1% is warranted in patients with renal impairment.

STORAGE AND STABILITY

Store at 4°C - 30°C. Protect from light. Discard the container at the end of treatment. Keep out of

the reach and sight of children.

DOSAGE FORMS, COMPOSITION AND PACKAGING

MINT-OLOPATADINE (olopatadine hydrochloride) ophthalmic solution is available in plastic dispensers containing 5 mL.

Each mL of MINT-OLOPATADINE solution contains: **Medicinal Ingredient:** 1.11 mg olopatadine hydrochloride equivalent to 1 mg olopatadine. **Preservative:** benzalkonium chloride 0.01%. **Non-medicinal ingredients:** sodium chloride, dibasic sodium phosphate dodecahydrate, hydrochloric acid/ sodium hydroxide (adjust pH), and purified water.

MINT-OLOPATADINE solution has a pH of approximately 7 and an osmolality of approximately 300 mOsm/kg.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Olopatadine hydrochloride

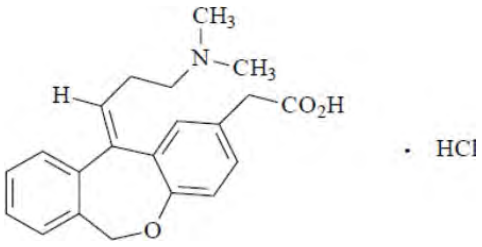
Chemical name:

(1) Dibenz[*b,e*]oxepin-2-acetic acid, 11-[3-(dimethylamino)propylidene]-6,11-dihydro-, hydrochloride, (Z)-

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

Molecular formula and molecular mass: $C_{21}H_{23}NO_3 \cdot HCl$; 373.88 g/mol

Structural formula:



Description:	White, crystalline powder
Solubility:	Sparingly soluble in methanol and water. Insoluble in chloroform.
pH (1% aqueous solution):	2.5

CLINICAL TRIALS

Study demographics and trial design

Table 1: Summary of trial design and patient demographics for clinical trials.

Study #	Trial design	Dosage, route of administration and duration	Study subjects (n=number)	Mean age (Range)	Gender
C-94-10	Randomized, double masked, placebo controlled, parallel group	Placebo, 0.01%, 0.05%, 0.1% and 0.15%; one ophthalmic drop 27 min., 6h and 8h prior to allergen challenge; 5 weeks.	98	37 years (18 – 64 yrs)	49 M 49 F
C-94-58	Triple masked, placebo controlled, randomized, contralateral eye comparison study.	Placebo, 0.05% and 0.1%; topical ocular administration; 4 weeks	60	46 years (18 – 72 yrs)	29 M 31 F
C-94-39	Triple masked, placebo controlled, randomized, contralateral eye comparison study.	Placebo, 0.05% and 0.1%; topical ocular administration; 4 weeks	120	39 years (18 – 80 yrs)	40 M 80 F

Study results

Table 2: Clinical trial study results.

Primary Endpoints	Associated value and statistical significance for Placebo or active control
C-94-10 Onset of action and duration of action for itching and redness.	Comparison between the four (4) olopatadine concentrations revealed a nonlinear dose relationship. All four (4) concentrations were statistically significant from placebo, however results showed the 0.1% olopatadine concentration to be most effective in reducing ocular itching and redness. At 3, 10 and 20 minutes, olopatadine 0.1% showed a mean point score reduction (range 0-4) in ocular itching compared to placebo of -1.72, -1.68 and -1.28 ($P \leq 0.05$), and a -2.72, -3.48 and -2.78 point score reduction (range 0-12) in ocular redness[†] compared to placebo ($P \leq 0.05$) when instilled 27 minutes prior to the conjunctival allergen challenge. Olopatadine 0.1% demonstrated a 6 hour duration of action when instilled 6 hours before the conjunctival allergen challenge. Results show a mean point score reduction (range 0-4) of -1.46, -1.70 and -1.07 in ocular itching compared to placebo ($P \leq 0.05$) at 3, 10 and 20 minutes following the allergen challenge. Similarly, ocular redness[†] scores showed a mean -1.52, -1.76 and -1.33 point score reduction (range 0-12) compared to placebo ($P \leq 0.05$) at 3, 10 and 20 minutes following the allergen challenge. Olopatadine 0.1% when instilled 8 hours before the conjunctival allergen challenge show a mean point score reduction (range 0-4) of -1.48, -1.62 and -0.92 in ocular itching compared to placebo ($P \leq 0.05$) at 3, 10 and 20 minutes following the onset-of-action challenge. Similarly, ocular redness[†] scores showed a mean -1.58, -1.78 and -1.42 point score reduction (range 0-12) compared to placebo ($P \leq 0.05$) at 3, 10 and 20 minutes following the onset-of-action challenge.
C-94-58 Onset of action and duration of action for itching and redness.	Olopatadine 0.1% was statistically superior to placebo in preventing ocular itching and redness with 3 minutes of the onset of action challenge. This difference from placebo persisted at the 8 hour duration of action challenge. At 3, 10 and 20 minutes post challenge, Olopatadine 0.1% showed a mean point score reduction (range 0-4) in ocular itching compared to placebo of -0.88, -1.19 and -1.07 ($P \leq 0.05$), and a -1.60, -1.69 and -1.38 point score reduction (range 0-12) in ocular redness[†] compared to placebo ($P \leq 0.05$), when one drop was instilled 27 minutes prior to the conjunctival allergen challenge. Olopatadine 0.1% when instilled 8 hours before the conjunctival allergen challenge show a mean point score reduction (range 0-4) of -0.37, -0.58 and -0.75 in ocular itching compared to placebo ($P \leq 0.05$) at 3, 10 and 20 minutes following the conjunctival allergen challenge. Ocular redness[†] scores showed a mean -0.13, -0.52 and -0.45 point score reduction (range 0-12) compared to placebo at 3, 10 and 20 minutes following the conjunctival allergen challenge.

Primary Endpoints	Associated value and statistical significance for Placebo or active control
C-94-39 Onset of action and duration of action for itching and redness.	Olopatadine 0.1% was statistically superior to placebo in preventing ocular itching and redness with 3 minutes of the onset of action challenge. This difference from placebo persisted at the 8 hour duration of action challenge. At 3, 10 and 20 minutes post challenge, Olopatadine 0.1% showed a mean point score reduction (range 0-4) in ocular itching compared to placebo of -1.25, -1.77 and -1.24 ($P \leq 0.05$), and a -2.18, -2.62 and -1.90 point score reduction (range 0-12) in ocular redness† compared to placebo ($P \leq 0.05$), when one drop was instilled 27 minutes prior to the conjunctival allergen challenge. Olopatadine 0.1% when instilled 8 hours before the conjunctival allergen challenge show a mean point score reduction (range 0-4) of -1.14, -1.29 and -1.06 in ocular itching compared to placebo ($P \leq 0.05$) at 3, 10 and 20 minutes following the onset-of-action challenge. Ocular redness† scores showed a mean -1.47, -1.23 and -0.87 point score reduction (range 0-12) compared to placebo ($P \leq 0.05$) at 3, 10 and 20 minutes following the conjunctival allergen challenge.

† Ocular redness is calculated as the sum of the ciliary redness (range 0-4), conjunctival redness (range 0-4) and episcleral redness (range 0-4) scores.

In well controlled clinical studies, olopatadine hydrochloride ophthalmic solution produced significantly less ocular discomfort (burning and stinging) compared to Acular® (ketorolac tromethamine) 0.5% Sterile Ophthalmic Solution and Livostin™ 0.05% (levocabastine hydrochloride ophthalmic suspension). Olopatadine hydrochloride ophthalmic solution also had significantly less effects on visual clarity relative to both Acular and Livostin™.

DETAILED PHARMACOLOGY

Olopatadine is an anti-allergic agent that exerts its effects through multiple distinct mechanisms of action. Olopatadine is a mast cell stabilizer and a potent, selective histamine H_1 antagonist (10) that inhibits the *in vivo* type 1 immediate hypersensitivity reaction. *In vitro* studies have demonstrated the ability of olopatadine to stabilize human conjunctival mast cells and inhibit immunologically-stimulated release of histamine. In addition, olopatadine inhibits the release of other mast cell inflammatory mediators [i.e., histamine, tryptase, prostaglandin D2 and TNFα (4,9,11,12)] as demonstrated in *in vitro* studies. Olopatadine is a selective histamine H_1 receptor antagonist *in vitro* and *in vivo* as demonstrated by its ability to inhibit histamine binding and histamine-stimulated vascular permeability in the conjunctiva following topical ocular administration (11). Olopatadine is also an inhibitor of pro-inflammatory cytokine secretion from human conjunctival epithelial cells (13). Decreased chemotaxis and inhibition of eosinophil activation has also been reported (6,8). Olopatadine is devoid of effects on alpha-adrenergic, dopamine, muscarinic type 1 and 2, and serotonin receptors.

Human Pharmacodynamics

Olopatadine had no observed effect on heart rate, cardiac conduction (PR and QRS interval duration), cardiac repolarization (QT duration) or wave form morphology relative to placebo in 2 double-masked, placebo controlled, 2-way crossover studies of 102 subjects given 5-mg oral doses of olopatadine every 12 hours for 2.5 days and 32 subjects given 20-mg oral doses twice-daily for 13.5 days [C-00-23 and C-02-54]. No clinically relevant or statistically significant changes in mean QTcF (determined to be the most appropriate heart correction formula for both

study populations) at steady-state from baseline were observed in either study. A categorical analysis of QTc (< 30 ms, 30 ms-60 ms, or > 60 ms) showed no statistically significant differences between olopatadine and placebo in both studies. An analysis of the maximal change from baseline in QTcF showed the difference was higher for placebo than for olopatadine.

Human Pharmacokinetics

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. These plasma concentrations were greater than 300 fold below those observed with a well-tolerated 20 mg oral multiple-dose regimen. In oral studies, olopatadine was found to be well absorbed. The half-life in plasma was 7-14 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.

TOXICOLOGY

The acute toxicity of olopatadine hydrochloride has been investigated in mice, rats and dogs. Mice and rats demonstrated that olopatadine hydrochloride was not an acute toxicity hazard with oral LD50 values greater than 1150 mg/kg and 3870 mg/kg for mice and rats, respectively.

Subchronic and chronic oral toxicity studies in rats and dogs demonstrated that the liver and kidney were target organs for olopatadine hydrochloride toxicity. In rats, ophthalmology and hematology parameters were unaffected following chronic administration of olopatadine hydrochloride. In chronic dog studies, ophthalmology, hematology, blood chemistry and organ weight parameters were unaffected by olopatadine hydrochloride administration.

A one-month topical ocular study was conducted with 0.1% (4 times a day) or 0.2% Olopatadine hydrochloride (4 and 5 times a day) Ophthalmic Solution in New Zealand White (NZW) rabbits. No signs of pharmacotoxicity were observed. Slit-lamp and indirect ocular evaluations and pachymetry revealed no treatment-related findings. Clinical pathology data and histopathology were unremarkable.

Chronic topical ocular studies were conducted with olopatadine hydrochloride in rabbits and monkeys. Administration of olopatadine hydrochloride at concentrations of 0.1, 0.5 and 1.0% QID to NZW rabbits elicited no signs of pharmacotoxicity. No treatment-related findings were observed during slit-lamp and indirect ocular evaluations and pachymetry measurements.

Clinical pathology data and histopathology were unremarkable. Similar findings were observed following six months of topical ocular administration of olopatadine hydrochloride at concentrations of 0.1, 0.2 and 0.5% QID to cynomolgus monkeys.

Antigenicity: Olopatadine hydrochloride was demonstrated to have a low potential for antigenicity when tested in mice and guinea pigs or in an *in vitro* passive hemagglutination test.

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PART III: CONSUMER INFORMATION

[Pr]MINT-OLOPATADINE
olopatadine hydrochloride ophthalmic solution, 0.1% w/v (as olopatadine hydrochloride)

This leaflet is part III of a three-part "Product Monograph" published when MINT-OLOPATADINE was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about MINT-OLOPATADINE. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
MINT-OLOPATADINE is used for the prevention and treatment of signs and symptoms of allergic conjunctivitis.

Allergic conjunctivitis: Some materials (allergens) like pollens, house dust or animal fur may cause allergic reactions resulting in itching, redness as well as swelling of the surface of your eye.

What it does:
MINT-OLOPATADINE is a medicine for treatment and control of allergic conditions of the eye. It works in two different ways by reducing and controlling the intensity of the allergic reaction.

When it should not be used:
MINT-OLOPATADINE should not be used if you are allergic (*hypersensitive*) to olopatadine hydrochloride, any of the other ingredients or components of the container (see **What the non-medicinal ingredients are).**

Tell your doctor if you have allergies.

Do not use MINT-OLOPATADINE in children under the age of three years.

What the medicinal ingredient is:
olopatadine hydrochloride

What the important non-medicinal ingredients are:
Preservative: benzalkonium chloride
Other ingredients include: dibasic sodium phosphate, purified water, and sodium chloride. Tiny amounts of hydrochloric acid or sodium hydroxide are sometimes added to maintain proper pH balance.

What dosage forms it comes in:
MINT-OLOPATADINE is a clear liquid (a solution) supplied in a plastic bottle with a screw cap containing 5 mL.

WARNINGS AND PRECAUTIONS

Pregnancy or breast-feeding: If you are pregnant, or planning to become pregnant, talk to your doctor before you use of MINT-OLOPATADINE.

If you are breast feeding, do not use MINT-OLOPATADINE; it may get into your breast milk.

Use of MINT-OLOPATADINE and use of contact lenses
- Do not wear contact lenses if your eyes are red.
- MINT-OLOPATADINE contains a preservative, benzalkonium chloride, which may cause eye irritation and is known to discolour soft contact lenses. Do not use the drops while wearing contact lenses.
- Remove your contacts before applying MINT-OLOPATADINE and wait at least 15 minutes before putting your contacts back in.

Use of MINT-OLOPATADINE with other eye drops or ointments
- If you use other eye drops, wait at least 5 minutes between putting in MINT-OLOPATADINE and the other drops.
- Apply eye ointments last.

Driving and using machines: You may find that your vision is blurred for a time just after you use MINT-OLOPATADINE. Do not drive or use machines until your vision is clear.

INTERACTIONS WITH THIS MEDICATION

Please tell your doctor if you are taking or have recently taken any other medicines, even products you have bought yourself without prescription or natural health products

There are no known drugs that interact with MINT-OLOPATADINE.

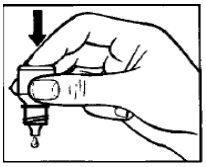
PROPER USE OF THIS MEDICATION

MINT-OLOPATADINE is an eye drop. Only use it in your eye(s).

If you are using other eye drops, wait at least 5 minutes before putting in MINT-OLOPATADINE and other eye drops. If you are using an eye ointment, you should apply it last.
Remove your contacts before applying MINT-OLOPATADINE and wait at least 15 minutes before putting your contacts back in.

Usual dose:
Adults and Children (3 years and older): 1 to 2 drops in each affected eye twice daily.

Instructions for Use:



1. Get the MINT-OLOPATADINE bottle and a mirror.
2. Wash your hands.
3. Twist off the cap, being careful not to touch the dropper tip.

4. Hold the bottle, pointing it down, between your thumb and middle finger.
5. Tilt your head back. Pull down your eyelid with a clean finger, until there is a 'pocket' between the eyelid and your eye. The drop will go in here (picture 1).
6. Bring the bottle tip close to the eye. Use the mirror if it helps. **Do not touch your eye or eyelid, or any surface with the dropper.** It could contaminate the drops, cause an eye infection and damage the eyes.
7. Gently press the base of the bottle with your forefinger to release one drop at a time. Do not squeeze the bottle: it is designed so that just a gentle press on the bottom is all that is required (picture 2).
8. If you use drops in both eyes, repeat the steps for the other eye.
9. Put the bottle cap firmly back on immediately after use.

Overdose:

If you think you have used too much MINT-OLOPATADINE, contact a health care professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

If you get too much in your eyes, rinse it all out with warm water. Don't put in any more drops until it's time for your next regular

Missed Dose:

If you forget to use MINT-OLOPATADINE, use a single drop as soon as you remember, and then go back to your regular routine. Do not use a double dose to make up for the one missed.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

A small number of people who use MINT-OLOPATADINE solution may get side effects. They can be unpleasant, but most of them disappear rapidly.

You can usually continue using the drops unless the effects are serious. If you're worried, talk to a doctor or pharmacist.

Side effects may include:

In the eye:
- eye problems such as dry, itchy, red, irritated or crusted eyes
- eye surface inflammation with or without surface damage
- eye discharge
- eye pain
- increased tear production
- eyelid redness, spasm, swelling or dryness
- sensitivity to light
- blurred vision
- staining in your eye
- burning, stinging or gritty feeling or a feeling as if something is trapped in the eye

Other areas of your body:
- headache
- dizziness
- fatigue or tiredness
- nasal dryness
- a dry mouth
- a change in your sense of taste
- nausea
- red or itchy skin

If you notice any side effects, other than discomfort, please inform your doctor or pharmacist.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Rare	**Allergic reactions:** Swelling of the mouth and throat, shortness of breath, hives, severe itching and rash			✓

This is not a complete list of side effects. For any unexpected effects while taking MINT-OLOPATADINE solution, contact your doctor or pharmacist.

HOW TO STORE IT

Store at room temperature or between 4°C - 30°C.
Protect from light. Throw away the bottle at the end of treatment.
Keep out of reach and sight of children.

REPORTING SIDE EFFECTS

You can report any suspected side effects associated with the use of health products to Health Canada by:

- **Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or**
- **Calling toll-free at 1-866-234-2345.**

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full Product Monograph, prepared for health professionals can be obtained by contacting the sponsor.

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