HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PATANASE® Nasal Spray safely and effectively. See full prescribing information for PATANASE Nasal Spray.
PATANASE (olopatadine hydrochloride) Nasal Spray
Initial U.S. Approval: 1996
----------INDICATIONS AND USAGE----------
PATANASE Nasal Spray is an H_1 receptor antagonist indicated for the relief of the symptoms of seasonal allergic rhinitis in patients 12 years of age and older. (1)
----------DOSAGE AND ADMINISTRATION----------
For intranasal use only.
The recommended dose of PATANASE Nasal Spray in patients 12 years and older is two sprays per nostril twice daily (2).
Priming Information: Prime PATANASE Nasal Spray before initial use and when PATANASE Nasal Spray has not been used for more than 7 days. (2.2)
----------DOSAGE FORMS AND STRENGTHS----------
Nasal spray 0.6%: 665 mcg of olopatadine hydrochloride in each 100- microliter spray. (3) Supplied as a 30.5 g bottle containing 240 sprays.
----------CONTRAINDICATIONS----------
None.
----------WARNINGS AND PRECAUTIONS----------
- Epistaxis, nasal ulceration, and nasal septal perforation. Monitor patients periodically for signs of adverse effects on the nasal mucosa. Avoid use in patients with nasal disease other than allergic rhinitis (5.1).
- Avoid engaging in hazardous occupations requiring complete mental alertness such as driving or operating machinery when taking PATANASE Nasal Spray (5.2).
- Avoid concurrent use of alcohol or other central nervous system depressants with PATANASE Nasal Spray (5.2).

----------ADVERSE REACTIONS----------
The most common adverse reactions (>1%) included bitter taste, headache, epistaxis, pharyngolaryngeal pain, post-nasal drip, cough, and urinary tract infection (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Alcon Laboratories, Inc. at 1-800-757-9195 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.
Revised: 2008

FULL PRESCRIBING INFORMATION*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Seasonal Allergic Rhinitis: PATANASE Nasal Spray is indicated for the relief of the symptoms of seasonal allergic rhinitis in patients 12 years of age and older.

2 DOSAGE AND ADMINISTRATION

Administer PATANASE Nasal Spray by the intranasal route only.

2.1 Adults and Adolescents 12 years of age and older: The recommended dosage is two sprays per nostril twice daily.

2.2 Administration Information
Priming: Before initial use, prime PATANASE Nasal Spray by releasing 5 sprays or until a fine mist appears. When PATANASE Nasal Spray has not been used for more than 7 days, re-prime by releasing 2 sprays. Avoid spraying PATANASE Nasal Spray into the eyes.

3 DOSAGE FORMS AND STRENGTHS

PATANASE Nasal Spray is a nasal spray solution supplied in a white plastic bottle with a metered-dose manual spray pump, a white nasal applicator, and a blue overcap. Each spray (100 microliters) delivers 665 mcg of olopatadine hydrochloride.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Local Nasal Effects
Epistaxis and Nasal Ulceration: In placebo (vehicle nasal spray)-controlled clinical trials of 2 weeks to 6 months duration, epistaxis and nasal ulcerations were reported [*see Adverse Reactions (6)*].

Nasal Septal Perforation:

Two placebo (vehicle nasal spray)-controlled long term (6 and 12 months) safety trials were conducted. In the 12-month safety trial, patients were treated with an investigational formulation of PATANASE Nasal Spray containing povidone (not the commercially marketed formulation) or a vehicle nasal spray containing povidone. Nasal septal perforations were reported in one patient treated with the investigational formulation of PATANASE Nasal Spray and 2 patients treated with the vehicle nasal spray. In a 6-month trial with PATANASE Nasal Spray, which does not contain povidone, there were no reports of nasal septal perforation [*see Adverse Reactions (6)*].

Before starting PATANASE Nasal Spray, conduct a nasal examination to ensure that patients are free of nasal disease other than allergic rhinitis. Perform nasal examinations periodically for signs of adverse effects on the nasal mucosa and consider stopping PATANASE Nasal Spray if patients develop nasal ulcerations.

5.2 Activities Requiring Mental Alertness
In clinical trials, the occurrence of somnolence has been reported in some patients taking PATANASE Nasal Spray [*see Adverse Reactions (6)*]. Patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness and motor coordination such as driving or operating machinery after administration of PATANASE Nasal Spray. Concurrent use of PATANASE Nasal Spray with alcohol or other central nervous system depressants should be avoided because additional reductions in alertness and additional impairment of central nervous system performance may occur.

6 ADVERSE REACTIONS

Use of PATANASE Nasal Spray has been associated with epistaxis, nasal ulceration, and somnolence [*see Warnings and Precautions (5.1 and 5.2)]*.

6.1 Clinical Trials Experience
The safety data described below reflect exposure to PATANASE Nasal Spray two sprays per nostril twice- daily in 1,491 patients 12 years of age and older (513 males and 978 females) with seasonal or perennial allergic rhinitis in 5 placebo (vehicle nasal spray)-controlled clinical trials of 2 weeks to 12 months duration. There were 1,180 patients (PATANASE Nasal Spray, 587; vehicle nasal spray, 593) that participated in 3 trials of 2 weeks duration, and 1,814 patients (PATANASE Nasal Spray, 904; vehicle nasal spray, 910) that participated in 2 long-term (6 months and 12 months) clinical trials. The racial and ethnic distribution of the 1,491 patients with exposure to PATANASE Nasal Spray was 76% white, 8% black, 12% Hispanic, and 3% other. The incidence of discontinuation due to adverse reactions in these controlled clinical trials was comparable for PATANASE Nasal Spray and vehicle nasal spray. Overall, 3.9% of the 1,491 patients across all 5 studies treated with PATANASE Nasal Spray and 3.2% of the 1,503 patients treated with vehicle nasal spray discontinued due to adverse reactions.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adults and Adolescents 12 years of Age and Older in Short-Term (2-week) Trials:

There were 1,180 patients (PATANASE Nasal Spray, 587; vehicle nasal spray, 593) with seasonal allergic rhinitis that participated in 3 clinical trials of 2 weeks duration. Table 1 presents the most common adverse reactions (0.9% or greater in patients treated with PATANASE Nasal Spray) that occurred more frequently in patients treated with PATANASE Nasal Spray compared with vehicle nasal spray.

Table 1: Adverse Reactions Occurring at an Incidence of 0.9% or Greater in Controlled Clinical Trials of 2 Weeks Duration with PATANASE Nasal Spray in Adolescent and Adult Patients 12 Years of Age and Older with Seasonal Allergic Rhinitis

Adverse Reaction	**PATANASE Nasal Spray N = 587**	**Vehicle Nasal Spray N = 593**
Bitter taste	75 (12.8%)	5 (0.8%)
Headache	26 (4.4%)	24 (4.0%)
Epistaxis	19 (3.2%)	10 (1.7%)
Pharyngolaryngeal Pain	13 (2.2%)	8 (1.3%)
Post-nasal drip	9 (1.5%)	5 (0.8%)

Cough	8 (1.4%)	3 (0.5%)
Urinary tract infection	7 (1.2%)	3 (0.5%)
CPK elevation	5 (0.9%)	2 (0.3%)
Dry mouth	5 (0.9%)	1 (0.2%)
Fatigue	5 (0.9%)	4 (0.7%)
Influenza	5 (0.9%)	1 (0.2%)
Nasopharyngitis	5 (0.9%)	4 (0.7%)
Somnolence	5 (0.9%)	2 (0.3%)
Throat irritation	5 (0.9%)	0 (0.0%)

There were no differences in the incidence of adverse reactions based on gender or race. Clinical trials did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger subjects.

Long-Term (6- and 12-month) Safety Trials:

In a 6-month, placebo (vehicle nasal spray)-controlled, safety trial, 445 patients 12 years of age and older with perennial allergic rhinitis were treated with PATANASE Nasal Spray 2 sprays per nostril twice daily, and 445 patients were treated with vehicle nasal spray. The most frequently reported adverse reaction was epistaxis, which occurred in 19% of patients treated with PATANASE Nasal Spray and 23% in patients treated with vehicle nasal spray. Epistaxis resulted in discontinuation of 0.7% of patients treated with PATANASE Nasal Spray and 0.2% of patients treated with vehicle nasal spray. Nasal ulcerations occurred in 9% of patients treated with PATANASE Nasal Spray and 6% of patients treated with vehicle nasal spray. Nasal ulcerations resulted in discontinuation of 0.4% of patients treated with PATANASE Nasal Spray and no patients treated with vehicle nasal spray. There were no patients with nasal septal perforation in either treatment group. Somnolence was reported in 1 patient treated with PATANASE Nasal Spray compared to none treated with vehicle nasal spray. Weight increase was reported in 5 patients treated with PATANASE Nasal Spray and in no patients treated with vehicle nasal spray.

In a 12-month, placebo (vehicle nasal spray)-controlled, safety trial, 459 patients 12 years of age and older with perennial allergic rhinitis were treated with 2 sprays per nostril of an investigational formulation of PATANASE Nasal Spray containing povidone (not the commercially marketed formulation) and 465 patients were treated with 2 sprays of a vehicle nasal spray containing povidone. Nasal septal perforations were reported in one patient treated with the investigational formulation of PATANASE Nasal Spray and 2 patients treated with the vehicle nasal spray. Epistaxis was reported in 19% of patients treated with the investigational formulation of PATANASE Nasal Spray and 12% of patients treated with vehicle nasal spray. Somnolence was reported in 3 patients treated with the investigational formulation of PATANASE Nasal Spray compared to 1 patient treated with vehicle nasal spray. Fatigue was reported in 5 patients treated with the investigational formulation of PATANASE Nasal Spray compared to 1 patient treated with vehicle nasal spray.

6.2 Post-Marketing Experience

In addition to the adverse reactions reported during clinical trials, adverse events have also been identified during post-approval use of olopatadine oral formulations (2.5 and 5 mg tablets) in other countries. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The most frequently reported adverse reaction was somnolence. Additional common adverse reactions included hypersensitivity reactions, dizziness, headache, malaise, thirst, abdominal pain, diarrhea, nausea, abnormal hepatic function, white blood cell disorders, occult blood in urine, and increased blood cholesterol.

7 DRUG INTERACTIONS

Drug-drug interaction studies were not conducted for PATANASE Nasal Spray. Drug interactions with inhibitors of liver enzymes are not anticipated because olopatadine is eliminated predominantly by renal excretion. Olopatadine did not inhibit the *in vitro* metabolism of specific substrates for CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4. Based on these data, drug interactions involving P450 inhibition are not expected. Due to the modest protein binding of olopatadine (55%), drug interactions through displacement from plasma proteins are not expected.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Pregnancy Category C:
No adequate and well-controlled studies in pregnant women have been conducted. Animal reproductive studies in rats and rabbits revealed treatment-related effects on fetuses or pups. Because animal studies are not always predictive of human responses, PATANASE Nasal Spray should be used in pregnant women only if the potential benefit to the mother justifies the potential risk to the embryo or fetus.

A decrease in the number of live fetuses was observed in rabbits and rats at the oral olopatadine doses approximately 88 times and 100 times the maximum recommended human dose (MRHD) and above, respectively, for adults on a mg/m^2 basis. In rats, viability and body weights of pups were reduced on day 4 post partum at the oral dose approximately 100 times the MRHD for adults on a mg/m^2 basis, but no effect on viability was observed at the dose approximately 35 times the MRHD for adults on a mg/m^2 basis.

8.3 Nursing Mothers
Olopatadine has been identified in the milk of nursing rats following oral administration. It is not known whether topical nasal administration could result in sufficient systemic absorption to produce detectable quantities in human breast milk. PATANASE Nasal Spray should be used by nursing mothers only if the potential benefit to the patient outweighs the potential risks to the infant.

8.4 Pediatric Use
Safety and effectiveness in pediatric patients below the age of 12 years have not yet been established.

8.5 Geriatric Use
Clinical studies of PATANASE Nasal Spray did not include sufficient numbers of patients aged 65 years and older to determine whether they respond differently from younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy.

10 OVERDOSAGE

There have been no reported overdosages with PATANASE Nasal Spray.

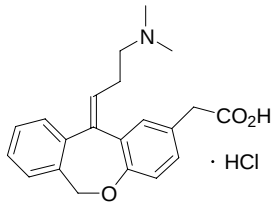
Acute overdosage with this dosage form is unlikely due to the configuration of the primary container closure system. However, symptoms of antihistamine overdose may include drowsiness in adults and, initially, agitation and restlessness, followed by drowsiness in children. There is no known specific antidote to PATANASE Nasal Spray. Should overdose occur, symptomatic or supportive treatment is recommended, taking into account any concomitantly ingested medications.

No mortality was observed in rats at an intranasal dose of 3.6 mg/kg (approximately 6 times the MRHD for adults on an mg/m^2 basis), or in dogs at an oral dose of 5 g/kg (approximately 28,000 times the MRHD for adults on a mg/m^2 basis). The oral median lethal dose (MLD) in mice and rats were 1,490 mg/kg and 3,870 mg/kg respectively (approximately 1,200 times and 6,500 times the MRHD for adults on a mg/m^2 basis, respectively).

For additional information about overdose treatment, call a poison control center (1-800-222-1222).

11 DESCRIPTION

PATANASE (olopatadine hydrochloride) Nasal Spray, 665 micrograms (mcg) is a metered-spray solution for intranasal administration. Olopatadine hydrochloride, the active component of PATANASE Nasal Spray, is a white, water-soluble crystalline powder. The chemical name for olopatadine hydrochloride is (Z)-11-[3-(dimethylamino)propylidene]-6,11-dihydrodibenz[b,e]oxepin-2-acetic acid hydrochloride. It has a molecular weight of 373.88, and its molecular formula is $C_{21}H_{23}NO_3 \cdot HCl$ with the following chemical structure:



PATANASE Nasal Spray contains 0.6% w/v olopatadine (base) in a nonsterile aqueous solution with pH of approximately 3.7. After initial priming (5 sprays), each metered spray from the nasal applicator delivers 100 microliters of the aqueous solution containing 665 mcg of olopatadine hydrochloride, which is equivalent to 600 mcg of olopatadine (base) *[see Dosage and Administration]*. PATANASE Nasal Spray also contains benzalkonium chloride (0.01%), dibasic sodium phosphate, edetate disodium, sodium chloride, hydrochloric acid and/or sodium hydroxide (to adjust pH), and purified water.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Olopatadine is an antihistamine with selective H_1 -receptor antagonist activity: its principal effects are mediated via inhibition of H_1 receptors. The antihistaminic activity of olopatadine has been documented in isolated tissues, animal models, and humans.

12.2 Pharmacodynamics
Cardiac effects**:** In a placebo-controlled cardiovascular safety study, 32 healthy volunteers received 20 mg oral solution of olopatadine twice daily for 14 days (8-fold greater daily dose than the recommended daily nasal dose). The mean QTcF (QT corrected by Fridericia's correction method for heart rate) change from baseline was -2.7 msec and -3.8 msec for olopatadine, and placebo, respectively. In this study, 8 subjects treated with olopatadine had a QTcF change from baseline of 30 – 60 msec, 1 subject had a QTcF change from baseline greater than 60 msec, and no subjects had QTcF values greater than 500 msec. Eight subjects treated with placebo had a QTcF change from baseline of 30 – 60 msec, no subjects had a QTcF change from baseline greater than 60 msec, and no subjects had QTcF values greater than 500 msec. In a 12-month study in 429 perennial allergic rhinitis patients treated with PATANASE Nasal Spray 2 sprays per nostril twice daily, no evidence of any effect of olopatadine hydrochloride on QT prolongation was observed.

12.3 Pharmacokinetics
The pharmacokinetic properties of olopatadine were studied after administration by the nasal, oral, intravenous, and topical ocular routes. Olopatadine exhibited linear pharmacokinetics across the routes studied over a large dose range.

Absorption:
Healthy Subjects: Olopatadine was absorbed with individual peak plasma concentrations observed between 30 minutes and 1 hour after twice daily intranasal administration of PATANASE Nasal Spray. The mean steady-state peak plasma concentration (C_{max}) of olopatadine was 16.0 ± 8.99 ng/mL. Systemic exposure as indexed by area under the curve (AUC_{0-12}) averaged 66.0 ± 26.8 ng·h/mL. The average absolute bioavailability of intranasal olopatadine is 57%. The mean accumulation ratio following multiple intranasal administration of PATANASE Nasal Spray was about 1.3.

Seasonal Allergic Rhinitis (SAR) Patients: Systemic exposure of olopatadine in SAR patients after twice daily intranasal administration of PATANASE Nasal Spray was comparable to that observed in healthy subjects. Olopatadine was absorbed with peak plasma concentrations observed between 15 minutes and 2 hours. The mean steady-state C_{max} was 23.3 ± 6.2 ng/mL and AUC_{0-12} averaged 78.0 ± 13.9 ng·h/mL.

Distribution: The protein binding of olopatadine was moderate at approximately 55% in human serum, and independent of drug concentration over the range of 0.1 to 1000 ng/mL. Olopatadine was bound predominately to human serum albumin.

Metabolism: Olopatadine is not extensively metabolized. Based on plasma metabolite profiles following oral administration of [^{14}C] olopatadine, at least six minor metabolites circulate in human plasma. Olopatadine accounts

for 77% of peak plasma total radioactivity and all metabolites amounted to <6% combined. Two of these have been identified as the olopatadine N-oxide and N-desmethyl olopatadine. In *in vitro* studies with cDNA-expressed human cytochrome P450 isoenzymes (CYP) and flavin-containing monooxygenases (FMO), N-desmethyl olopatadine (Ml) formation was catalyzed mainly by CYP3A4, while olopatadine N-oxide (M3) was primarily catalyzed by FMO1 and FMO3. Olopatadine at concentrations up to 33,900 ng/mL did not inhibit the *in vitro* metabolism of specific substrates for CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4. The potential for olopatadine and its metabolites to act as inducers of CYP enzymes has not been evaluated.

Elimination: The plasma elimination half-life of olopatadine is 8 to 12 hours. Olopatadine is mainly eliminated through urinary excretion. Approximately 70% of a [^{14}C] olopatadine hydrochloride oral dose was recovered in urine with 17% in the feces. Of the drug-related material recovered within the first 24 hours in the urine, 86% was unchanged olopatadine with the balance comprised of olopatadine N-oxide and N-desmethyl olopatadine.

Special Population:
Hepatic Impairment: 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 PATANASE Nasal Spray is warranted in patients with hepatic impairment.

Renal Impairment: The mean C_{max} values for olopatadine following single intranasal doses were not markedly different between healthy subjects (18.1 ng/mL) and patients with mild, moderate and severe renal impairment (range 15.5 to 21.6 ng/mL). Mean plasma AUC_{0-12} was two-fold higher in patients with severe impairment (creatinine clearance <30 mL/min/1.73 m^2). In these patients, peak steady-state plasma concentrations of olopatadine are approximately 10-fold lower than those observed after higher 20 mg oral doses, twice daily, which were safe and well-tolerated. These findings indicate that no adjustment of the dosing regimen of PATANASE Nasal Spray is warranted in patients with renal impairment.

Gender: The mean systemic exposure (C_{max} and AUC_{0-12}) in female SAR patients following multiple administration of olopatadine was 40% and 27% higher, respectively than those values observed in male SAR patients.

Race: The effects of race on olopatadine pharmacokinetics have not been adequately investigated.

Age: The effects of age on olopatadine pharmacokinetics have not been adequately investigated.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Olopatadine administered orally was not carcinogenic in mice and rats at doses of up to 500 mg/kg/day and 200 mg/kg/day, respectively (approximately 420 and 340 times the MRHD for adults by intranasal administration on a mg/m^2 basis, respectively).

There was no evidence of genotoxicity when olopatadine was tested in an *in vitro* bacteria reverse mutation test (Ames), an *in vitro* mammalian chromosome aberration assay or an *in vivo* mouse micronucleus test.

Olopatadine administered orally to male and female rats at dose of 400 mg/kg/day, (approximately 680 times the MRHD for adults on a mg/m^2 basis) resulted in a decrease in the fertility index and reduced implantation rate. No effects on fertility were observed at dose of 50 mg/kg/day (approximately 85 times the MRHD for adults on a mg/m^2 basis).

13.2 Animal Toxicology

Reproductive Toxicology Studies
Olopatadine was not teratogenic in rabbits and rats at oral doses of up to 400 or 600 mg/kg/day, respectively (approximately 1,400 and 1,000 times the MRHD for adults on a mg/m^2 basis, respectively). However, a decrease in the number of live fetuses was observed in rabbits at the oral olopatadine doses of 25 mg/kg (approximately 88 times the MRHD for adults on a mg/m^2 basis) and above, and in rats at oral doses of 60 mg/kg (approximately 100 times the MRHD for adults on a mg/m^2 basis) and above. In rats, viability and body weights of pups were reduced on day 4 post partum at the oral doses of 60 mg/kg (approximately 100 times the MRHD for adults on a mg/m^2 basis) and above, but no effect on viability was observed at the dose of 20 mg/kg (approximately 35 times the MRHD for adults on a mg/m^2 basis).

14 CLINICAL STUDIES

14.1 Seasonal Allergic Rhinitis

Adult and Adolescent Patients 12 Years of Age and Older:
The efficacy and safety of PATANASE Nasal Spray were evaluated in three randomized, double blind, parallel group, multicenter, placebo (vehicle nasal spray)-controlled clinical trials of 2 weeks duration in adult and adolescent patients, 12 years of age and older with symptoms of seasonal allergic rhinitis. The three clinical trials were conducted in the United States and included 1,598 patients (556 males, and 1,042 females) 12 years of age and older. In these three trials 587 patients were treated with PATANASE Nasal Spray 0.6%, 418 patients were treated with PATANASE Nasal Spray 0.4%, and 593 patients were treated with vehicle nasal spray. Assessment of efficacy was based on patient recording of 4 individual nasal symptoms (nasal congestion, rhinorrhea, itchy nose, and sneezing) on a 0 to 3 categorical severity scale (0 = absent, 1 = mild, 2 = moderate, 3 = severe) as reflective or instantaneous scores. Reflective scoring required patients to record symptom severity over the previous 12 hours; the instantaneous scoring required patients to record symptom severity at the time of recording. The primary efficacy endpoint was the difference from placebo in the percent change from baseline in the sum of morning and evening reflective total nasal symptom score (rTNSS) averaged for the 2-week treatment period. In all 3 trials, patients treated with PATANASE Nasal Spray, two sprays per nostril, twice-daily, exhibited statistically significantly greater decreases in rTNSS compared to vehicle nasal spray. Results for the rTNSS from two representative trials are shown in Table 2.

Table 2: Mean Reflective Total Nasal Symptom Score (rTNSS) Over 2 Weeks in Seasonal Allergic Rhinitis Trials

	Treatment	N	Baseline	Change from Baseline	Difference from Placebo		
					Estimate	95% CI	p-value
Study 1	PATANASE Nasal Spray 0.6%	183	8.71	-3.63	-0.96	(-1.42, -0.51)	<0.0001
	PATANASE Nasal Spray 0.4%	188	8.90	-3.38	-0.71	(-1.17, -0.26)	0.0023
	Vehicle Nasal Spray	191	8.75	-2.67			
Study 2	PATANASE Nasal Spray 0.6%	220	9.17	-2.90	-0.98	(-1.37, -0.59)	<0.0001
	PATANASE Nasal Spray 0.4%	228	9.26	-2.63	-0.72	(-1.11, -0.33)	0.0003
	Vehicle Nasal Spray	223	9.07	-1.92			

In the 2-week seasonal allergic trials, onset of action was also evaluated by instantaneous TNSS assessments twice-daily after the first dose of study medication. In these trials, onset of action was seen after 1 day of dosing. Onset of action was evaluated in three environmental exposure unit studies with single doses of PATANASE Nasal Spray. In these studies, patients with seasonal allergic rhinitis were exposed to high levels of pollen in the environmental exposure unit and then treated with either PATANASE Nasal Spray or vehicle nasal spray, two sprays in each nostril, after which they self-reported their allergy symptoms hourly as instantaneous scores for the subsequent 12 hours. PATANASE Nasal Spray 0.6% was found to have an onset of action of 30 minutes after dosing in the environmental exposure unit.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

PATANASE Nasal Spray, 665 mcg is supplied in a white plastic bottle with a metered-dose manual spray pump, a white nasal applicator and a blue overcap in a box of 1 (NDC 0065-0332-30). Each trade size bottle contains 30.5 g of clear, colorless liquid and will provide 240 metered sprays. After priming [*see Dosage and Administration (2)*], each spray delivers a fine mist containing 665 mcg of olopatadine hydrochloride in 100 microliters of formulation through the nozzle.

Before initial use, prime PATANASE Nasal Spray by releasing 5 sprays or until a fine mist appears. After periods of non-use greater than 7 days, re-prime PATANASE Nasal Spray by releasing 2 sprays. The correct amount of medication cannot be assured before the initial priming and after 240 sprays have been used, even though the bottle

is not completely empty. The nasal device should be discarded after 240 sprays (enough for 30 days of dosing) have been used.

Net content 30.5 g, 240 sprays: NDC 0065-0332-30 (trade size)

16.2 Storage
Store at 4° to 25° C (39° to 77° F). Rx Only.

17 PATIENT COUNSELING INFORMATION

See FDA-approved Patient Labeling accompanying the product.

17.1 Local Nasal Effects and Other Common Adverse Reactions
Patients should be informed that treatment with PATANASE Nasal Spray may lead to adverse reactions, which include epistaxis and nasal ulcerations. [*see Warnings and Precautions (5.1*)] Other common adverse reactions reported with use of PATANASE Nasal Spray include bitter taste, headache, pharyngolaryngeal pain, post-nasal drip, cough, and urinary tract infection [*see Adverse Reactions (6*)].

17.2. Activities Requiring Mental Alertness
Somnolence has been reported in some patients taking PATANASE Nasal Spray. Patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness and motor coordination such as driving or operating machinery after administration of PATANASE Nasal Spray [*see Warnings and Precautions (5.2*)].

17.3 Concurrent Use of Alcohol and other Central Nervous System Depressants
Concurrent use of PATANASE Nasal Spray with alcohol or other central nervous system depressants should be avoided because additional reductions in alertness and additional impairment of central nervous system performance may occur [*see Warnings and Precautions (5.2*)].

17.4. Keep Spray Out of Eyes
Patients should be informed to avoid spraying PATANASE Nasal Spray in their eyes.

Revised: March 2008

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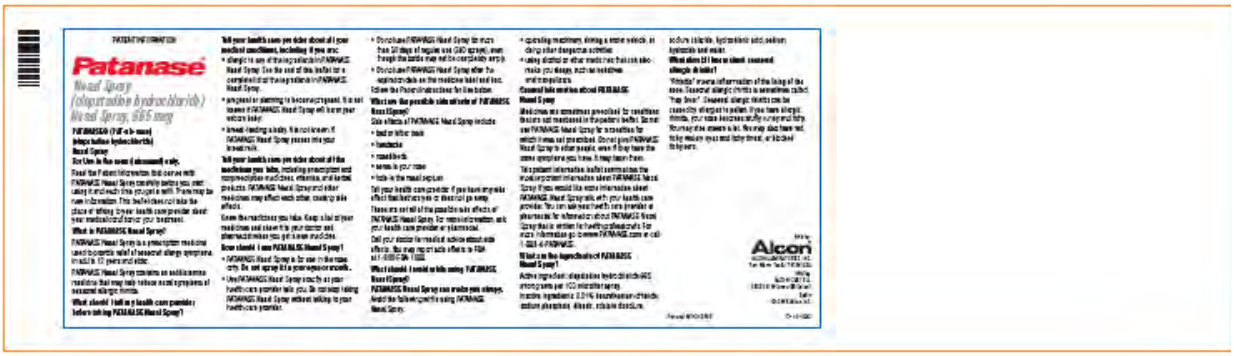

PATIENT INFORMATION

Patanase®

Nasal Spray

(olopatadine hydrochloride)

Nasal Spray, 665 mcg

PATANASE® (PAT-a-nase)

(olopatadine hydrochloride)

Nasal Spray

For Use in One Nostril Only

Read the Patient Information that comes with PATANASE Nasal Spray carefully before you start using it and each time you get a refill. There may be new information. This leaflet does not take the place of talking to your health care provider about your medical condition or your treatment.

What is PATANASE Nasal Spray?

PATANASE Nasal Spray is a prescription medicine used to control relief of seasonal allergy symptoms in adults 18 years and older.

PATANASE Nasal Spray contains an antihistamine medicine that may help relieve nasal symptoms of seasonal allergic rhinitis.

What should I tell my health care provider before using PATANASE Nasal Spray?

Tell your health care provider about all your medical conditions, including if you are:

- allergic to any of the ingredients in PATANASE Nasal Spray. See the end of this leaflet for a complete list of the ingredients in PATANASE Nasal Spray.
- pregnant or planning to become pregnant. It is not known if PATANASE Nasal Spray will harm your unborn baby.
- breast-feeding a baby. It is not known if PATANASE Nasal Spray passes into your breast milk.

Tell your health care provider about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal products. PATANASE Nasal Spray and other medicines may affect each other, causing side effects.

Know the medicines you take. Keep a list of your medicines and show it to your doctor and pharmacist when you get a new medicine.

How should I use PATANASE Nasal Spray?

- PATANASE Nasal Spray is for use in the nose only. Do not spray it in your eyes or mouth.
- Use PATANASE Nasal Spray exactly as your healthcare provider tells you. Do not stop using PATANASE Nasal Spray without talking to your healthcare provider.
- Do not use PATANASE Nasal Spray for more than 30 days of regular use (240 sprays), even though the bottle may not be completely empty.
- Do not use PATANASE Nasal Spray after the expiration date on the medicine label and box. Do not use the Pump Instructions' for this bottle.

What are the possible side effects of PATANASE Nasal Spray?

Side effects of PATANASE Nasal Spray include:

- bad or bitter taste
- headache
- nosebleeds
- sores in your nose
- hole in the nasal septum

Tell your health care provider if you have any side effect that bothers you or does not go away.

These are not all of the possible side effects of PATANASE Nasal Spray. For more information, ask your health care provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

What should I avoid while using PATANASE Nasal Spray?

PATANASE Nasal Spray can make you sleepy. Avoid the following until you know how PATANASE Nasal Spray affects you:

- operating machinery, driving a motor vehicle, or doing other dangerous activities
- using alcohol or other medicines that can also make you sleepy, such as sedatives and tranquilizers

General information about PATANASE Nasal Spray

Medicines are sometimes prescribed for conditions that are not mentioned in this patient leaflet. Do not use PATANASE Nasal Spray for a condition for which it was not prescribed. Do not give PATANASE Nasal Spray to other people, even if they have the same symptoms you have. It may harm them.

This patient information leaflet summarizes the most important information about PATANASE Nasal Spray. If you would like more information, talk to PATANASE Nasal Spray with your health care provider. You can ask your health care provider or pharmacist for information about PATANASE Nasal Spray that is written for health professionals. For more information go to www.PATANASE.com or call 1-800-4-PATANASE.

What are the ingredients in PATANASE Nasal Spray?

Active ingredient: olopatadine hydrochloride 0.665 mg/spray per 100 microliter spray.

Inactive ingredients: 0.01% benzalkonium chloride, sodium phosphate, dibasic, edetate disodium, sodium chloride, hydrochloric acid, sodium hydroxide and water.

What does it mean if I have a nasal seasonal allergic rhinitis?

"Rhinitis" means inflammation of the lining of the nose. Seasonal allergic rhinitis is sometimes called "hay fever". Seasonal allergic rhinitis can be caused by allergens to pollen. If you have allergic rhinitis, you have become sensitive to material that flows up the stream a bit. You may also have red, itchy, watery eyes and itchy throat, or blocked or leaky nose.

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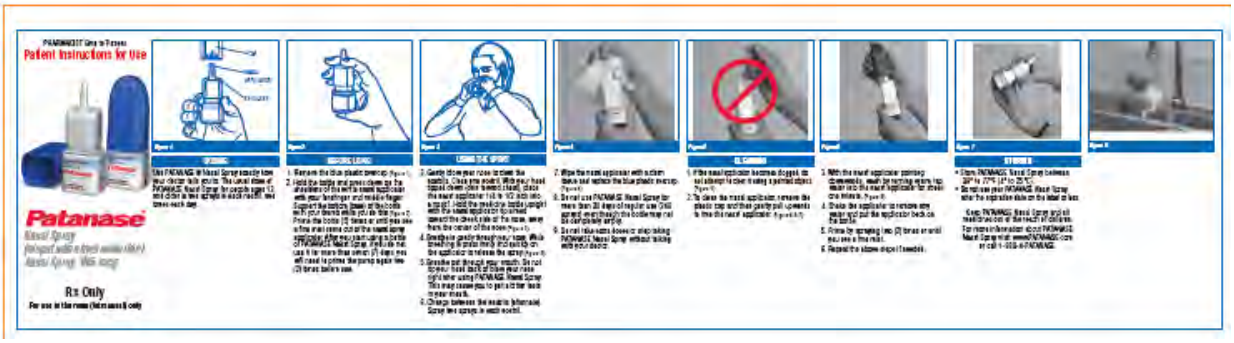

Patient Instructions for Use

Patanase®

Nasal Spray

(olopatadine hydrochloride)

Nasal Spray, 665 mcg

Rx Only

For use in the nose (intranasal) only

Figure 1

Figure 2

Figure 3

Figure 4

Figure 5

Figure 6

Figure 7

Figure 8

PRIMING

Use PATANASE® Nasal Spray exactly how your doctor tells you to. The usual dose of PATANASE Nasal Spray for people ages 12 and older is two sprays in each nostril, one time each day.

BEFORE USING

1. Remove the blue plastic protector. (Figure 1)
2. Hold the bottle and press down on the dropdown of the metal nasal application with your forefinger and middle finger. Support the bottom (base) of the bottle with your thumb while you do this. (Figure 2) Prime the bottle (3) times or until you see a fine mist come out of the nasal spray nozzle. After you start using it, PATANASE Nasal Spray medicine will last for more than seven (7) days, you will need to prime the pump again two (2) times before use.

USING THE SPRAY

3. Gently blow your nose to clear the nostrils. Close one nostril. While your head tipped down slightly forward, place the nasal applicator tube in YOU and into a nostril. Hold the medicine bottle upright with the nasal applicator to your head. Spread the cheek side of the nose, away from the center of the nose. (Figure 3)
4. Breathe in gently through your nose, while breathing in gently start to push on the applicator to release the spray. (Figure 4)
5. Breathe out through your mouth. Do not breathe your head back or blow your nose right after using PATANASE Nasal Spray. This may cause you to get a bit the back in your nose.
6. Change between the nostrils (alternate) Spray two sprays in each nostril.

Figure 5

Figure 6

Figure 7

Figure 8

7. Wipe the nasal applicator with a clean tissue and replace the blue plastic protector. (Figure 5)
8. Do not use PATANASE Nasal Spray for more than 30 days of regular use (240 sprays) even though the bottle may not be completely empty.
9. Do not take extra doses or stop taking PATANASE Nasal Spray without talking with your doctor.

- If the nasal applicator becomes clogged, do not attempt to clear it using a pointed object. (Figure 6)
- To clean the nasal applicator, remove the plastic cap and then gently pull upwards to free the nasal applicator. (Figure 6 & 7)

1. With the nasal applicator pointing downwards, wash (or running warm tap water into the nasal applicator for about one minute. (Figure 8)
2. Shake the applicator to remove any water and put the applicator back on the bottle.
3. Prime by spraying two (2) times or until you see a fine mist.
4. Repeat the above steps if needed.

STORAGE

- Store PATANASE Nasal Spray between 20° to 77°F (4° to 25°C).
- Keep out of the reach of children.

For more information about PATANASE Nasal Spray visit www.PATANASE.com or call 1-800-4-PATANASE.

Keep PATANASE Nasal Spray and all medicines out of the reach of children.