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)*].

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%)

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:

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