HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ASTEPRO® Nasal Spray safely and effectively. See full prescribing information for ASTEPRO Nasal Spray.

ASTEPRO (azelastine hydrochloride) Nasal Spray 0.1%
ASTEPRO (azelastine hydrochloride) Nasal Spray 0.15%

Initial U.S. Approval: 1996

----------**INDICATIONS AND USAGE**----------
ASTEPRO Nasal Spray is an H_1 receptor antagonist indicated for the relief of the symptoms of seasonal and perennial allergic rhinitis in patients 12 years of age and older. (1.1)

----------**DOSAGE AND ADMINISTRATION**---------
For intranasal use only (2.3).

Seasonal allergic rhinitis:
• ASTEPRO Nasal Spray 0.1% and 0.15%: 1 or 2 sprays per nostril twice daily in adults and adolescents 12 years of age and older (2.1)
• ASTEPRO Nasal Spray 0.15%: 2 sprays per nostril once daily in adults and adolescents 12 years of age and older (2.1)

Perennial allergic rhinitis:
• ASTEPRO Nasal Spray 0.15%: 2 sprays per nostril twice daily in adults and adolescents 12 years of age and older (2.2)

• Prime ASTEPRO Nasal Spray before initial use and when it has not been used for 3 or more days. (2.3)

----------**DOSAGE FORMS AND STRENGTHS**-------
ASTEPRO Nasal Spray 0.1%: 137 mcg of azelastine hydrochloride in each 0.137 mL spray (3).
ASTEPRO Nasal Spray 0.15%: 205.5 mcg of azelastine hydrochloride in each 0.137 mL spray (3).

----------**CONTRAINDICATIONS**----------
None.

----------**WARNINGS AND PRECAUTIONS**----------
• Somnolence may occur. Avoid engaging in hazardous occupations requiring complete mental alertness such as driving or operating machinery when taking ASTEPRO Nasal Spray (5.1)
• Avoid concurrent use of alcohol or other central nervous system (CNS) depressants with ASTEPRO Nasal Spray because further decreased alertness and impairment of CNS performance may occur (5.1)

----------**ADVERSE REACTIONS**----------
The most common adverse reactions (≥2% incidence) are: bitter taste, nasal discomfort, epistaxis, headache, fatigue, somnolence and sneezing (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact MEDA Pharmaceuticals Inc. at 1-800-526-3840 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

----------**USE IN SPECIFIC POPULATIONS**----------
• Pregnancy: Based on animal data, may cause fetal harm (8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA approved patient labeling.

Revised mm/yy

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Allergic Rhinitis

ASTEPRO Nasal Spray 0.1% and 0.15% is indicated for the relief of the symptoms of seasonal and perennial allergic rhinitis in patients 12 years of age and older.

2 DOSAGE AND ADMINISTRATION

2.1 Seasonal Allergic Rhinitis

The recommended dose of ASTEPRO Nasal Spray 0.1% and 0.15% is 1 or 2 sprays per nostril twice daily for seasonal allergic rhinitis. ASTEPRO Nasal Spray 0.15% may also be administered as 2 sprays per nostril once daily.

2.2 Perennial Allergic Rhinitis

The recommended dose of ASTEPRO Nasal Spray 0.15% for perennial allergic rhinitis is 2 sprays per nostril twice daily.

2.3 Important Administration Instructions

Administer ASTEPRO Nasal Spray by the intranasal route only.

Priming: Prime ASTEPRO Nasal Spray before initial use by releasing 6 sprays or until a fine mist appears. When ASTEPRO Nasal Spray has not been used for 3 or more days, reprime with 2 sprays or until a fine mist appears. Avoid spraying ASTEPRO Nasal Spray into the eyes.

3 DOSAGE FORMS AND STRENGTHS

ASTEPRO Nasal Spray is a nasal spray solution. Each spray of ASTEPRO Nasal Spray 0.1% delivers a volume of 0.137 mL solution containing 137 mcg of azelastine hydrochloride. Each spray of ASTEPRO Nasal Spray 0.15% delivers a volume of 0.137 mL solution containing 205.5 mcg of azelastine hydrochloride.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Activities Requiring Mental Alertness

In clinical trials, the occurrence of somnolence has been reported in some patients taking ASTEPRO Nasal Spray [*see Adverse Reactions (6.1)*]. Patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness and motor coordination such as operating machinery or driving a motor vehicle after administration of ASTEPRO Nasal Spray. Concurrent use of ASTEPRO 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 Drug Interactions (7.1)*].

6 ADVERSE REACTIONS

Use of ASTEPRO Nasal Spray has been associated with somnolence [*see Warnings and Precautions (5.1)*].

6.1 Clinical Trials Experience

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

ASTEPRO Nasal Spray 0.1%

The safety data described below reflect exposure to ASTEPRO Nasal Spray 0.1% in 713 patients 12 years of age and older from 2 clinical trials of 2 weeks to 12 months duration. In a 2 week, double-blind, placebo-controlled, and active controlled (Astelin® Nasal Spray; azelastine hydrochloride) clinical trial, 285 patients (115 males and 170 females) 12 years of age and older with seasonal allergic rhinitis were treated with ASTEPRO Nasal Spray 0.1% one or two sprays per nostril daily. In the 12 month open-label, active controlled (Astelin Nasal Spray) clinical trial, 428 patients (207 males and 221 females) 12 years of age and older with perennial allergic rhinitis and/or nonallergic rhinitis were treated with ASTEPRO Nasal Spray 0.1% two sprays per nostril twice daily. The racial and ethnic distribution for the 2 clinical trials was 82% white, 8% black, 6% Hispanic, 3% Asian, and <1% other.

Adults and Adolescents 12 Years of Age and Older

In the two week clinical trial, 835 patients 12 years of age and older with seasonal allergic rhinitis were treated with one of six treatments: one spray per nostril of either ASTEPRO Nasal Spray 0.1%, Astelin Nasal Spray or placebo twice daily; or 2 sprays per nostril of ASTEPRO Nasal Spray 0.1%, Astelin Nasal Spray, or placebo twice daily. Overall, adverse reactions were more common in the ASTEPRO Nasal Spray 0.1% treatment groups (21-28%) than in the placebo groups (16-20%). Overall, less than 1% of patients discontinued due to adverse reactions and withdrawal due to adverse reactions was similar among the treatment groups.

Table 1 contains adverse reactions reported with frequencies greater than or equal to 2% and more frequently than placebo in patients treated with ASTEPRO Nasal Spray 0.1% in the controlled clinical trial described above.

Table 1. Adverse Reactions Reported in ≥2% Incidence in a Placebo-Controlled Trial of 2 Weeks Duration with ASTEPRO Nasal Spray 0.1% in Adult and Adolescent Patients with Seasonal Allergic Rhinitis

	1 spray twice daily			2 sprays twice daily		
	ASTEPRO Nasal Spray 0.1% (N=139)	Astelin Nasal Spray (N=137)	Vehicle Placebo (N=137)	ASTEPRO Nasal Spray 0.1% (N=146)	Astelin Nasal Spray (N=137)	Vehicle Placebo (N=138)
Bitter Taste	8 (6%)	13 (10%)	2 (2%)	10 (7%)	11 (8%)	3 (2%)
Epistaxis	3 (2%)	8 (6%)	3 (2%)	4 (3%)	3 (2%)	0 (0%)
Headache	2 (1%)	5 (4%)	1 (<1%)	4 (3%)	3 (2%)	1 (<1%)
Nasal Discomfort	0 (0%)	3 (2%)	1 (<1%)	2 (1%)	6 (4%)	0 (0%)
Fatigue	0 (0%)	1 (<1%)	1 (<1%)	3 (2%)	3 (2%)	1 (<1%)
Somnolence	2 (1%)	2 (2%)	0 (0%)	3 (2%)	2 (1%)	0 (0%)

Long-Term (12 Month) Safety Trial:

In the 12 month, open-label, active-controlled, long-term safety trial, 862 patients 12 years of age and older with perennial allergic and/or nonallergic rhinitis were treated with ASTEPRO Nasal Spray 0.1% two sprays per nostril twice daily or Astelin Nasal Spray two sprays per nostril twice daily. The most frequently reported adverse reactions were

headache, bitter taste, epistaxis, and nasopharyngitis and were generally similar between treatment groups. Focused nasal examinations were performed and showed that the incidence of nasal mucosal ulceration in each treatment group was approximately 1% at baseline and approximately 1.5% throughout the 12 month treatment period. In each treatment group, 5-7% of patients had mild epistaxis. No patients had reports of nasal septal perforation or severe epistaxis. Twenty-two patients (5%) treated with ASTEPRO Nasal Spray 0.1% and 17 patients (4%) treated with Astelin Nasal Spray discontinued from the trial due to adverse events.

ASTEPRO Nasal Spray 0.15%

The safety data described below reflect exposure to ASTEPRO Nasal Spray 0.15% in 1858 patients (12 years of age and older) with seasonal or perennial allergic rhinitis from 8 clinical trials of 2 weeks to 12 months duration. In 7 double-blind, placebo-controlled clinical trials of 2 to 4 weeks duration, 1544 patients (560 males and 984 females) with seasonal or perennial allergic rhinitis were treated with ASTEPRO Nasal Spray 0.15% two sprays per nostril once or twice daily. In the 12 month open-label, active-controlled clinical trial, 466 patients (156 males and 310 females) with perennial allergic rhinitis were treated with ASTEPRO Nasal Spray 0.15% two sprays per nostril twice daily. Of these 466 patients, 152 had participated in the 4-week placebo-controlled perennial allergic rhinitis clinical trials. The racial distribution for the 8 clinical trials was 80% white, 13% black, 2% Asian, and 5% other.

Adults and Adolescents 12 Years of Age and Older

In the 7 placebo controlled clinical trials of 2 to 4 week duration, 2343 patients with seasonal allergic rhinitis and 540 patients with perennial allergic rhinitis were treated with two sprays per nostril of either ASTEPRO Nasal Spray 0.15% or placebo once or twice daily. Overall, adverse reactions were more common in the ASTEPRO Nasal Spray 0.15% treatment groups (16-31%) than in the placebo groups (11-24%). Overall, less than 2% of patients discontinued due to adverse reactions and withdrawal due to adverse reactions was similar among the treatment groups.

Table 2 contains adverse reactions reported with frequencies greater than or equal to 2% and more frequently than placebo in patients treated with ASTEPRO Nasal Spray 0.15% in the seasonal and perennial allergic rhinitis controlled clinical trials.

Table 2. Adverse Reactions with ≥2% Incidence in Placebo-Controlled Trials of 2 to 4 Weeks' Duration with ASTEPRO Nasal Spray 0.15% in Adult and Adolescent Patients With Seasonal or Perennial Allergic Rhinitis

	2 sprays twice daily		2 sprays once daily	
	ASTEPRO Nasal Spray 0.15% (N=523)	Vehicle Placebo (N=523)	ASTEPRO Nasal Spray 0.15% (N=1021)	Vehicle Placebo (N=816)
Bitter Taste	31 (6%)	5 (1%)	38 (4%)	2 (<1%)
Nasal Discomfort	18 (3%)	12 (2%)	37 (4%)	7 (1%)
Epistaxis	5 (1%)	7 (1%)	21 (2%)	14 (2%)
Sneezing	9 (2%)	1 (<1%)	14 (1%)	0 (0%)

In the above trials, somnolence was reported in <1% of patients treated with ASTEPRO Nasal Spray 0.15% (11 of 1544) or vehicle placebo (1 of 1339).

Long-Term (12 Month) Safety Trial:

In the 12 month, open-label, active-controlled, long-term safety trial, 466 patients (12 years of age and older) with perennial allergic rhinitis were treated with ASTEPRO Nasal Spray 0.15% two sprays per nostril twice daily and 237 patients were treated with mometasone nasal spray two sprays per nostril once daily. The most frequently reported adverse reactions (>5%) with ASTEPRO Nasal Spray 0.15% were bitter taste, headache, sinusitis, and epistaxis. Focused nasal examinations were performed and no nasal ulcerations or septal perforations were observed. In each treatment group, approximately 3% of patients had mild epistaxis. No patients had reports of severe epistaxis. Fifty-four patients (12%) treated with ASTEPRO Nasal Spray 0.15% and 17 patients (7%) treated with mometasone nasal spray discontinued from the trial due to adverse events.

6.2 Postmarketing Experience

The following adverse reactions have been identified during the post approval use of the Astelin brand of azelastine hydrochloride 0.1% nasal spray (total daily dose 0.55 mg to 1.1 mg). Because these reactions 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. Adverse reactions reported include the following: anaphylactoid reaction, application site irritation, atrial fibrillation, blurred vision, chest pain, confusion, dizziness, dyspnea, facial edema, hypertension, involuntary muscle contractions, nervousness, palpitations, paresthesia, parosmia, paroxysmal sneezing, pruritus, rash, disturbance or loss of sense of smell and/or taste, tachycardia, tolerance, urinary retention, and xerophthalmia.

7 DRUG INTERACTIONS

7.1 Central Nervous System Depressants

Concurrent use of ASTEPRO Nasal Spray with alcohol or other central nervous system depressants should be avoided because reductions in alertness and impairment of central nervous system performance may occur [*see Warnings and Precautions (5.1)*].

7.2 Erythromycin and Ketoconazole

Interaction studies investigating the cardiac effects, as measured by the corrected QT interval (QTc), of concomitantly administered oral azelastine hydrochloride and erythromycin or ketoconazole were conducted. Oral erythromycin (500 mg three times daily for 7 days) had no effect on azelastine pharmacokinetics or QTc based on analyses of serial electrocardiograms. Ketoconazole (200 mg twice daily for 7 days) interfered with the measurement of azelastine plasma concentrations on the analytic HPLC; however, no effects on QTc were observed [*see Clinical Pharmacology (12.2) and (12.3)*].

7.3 Cimetidine

Cimetidine (400 mg twice daily) increased the mean C_{max} and AUC of orally administered azelastine hydrochloride (4 mg twice daily) by approximately 65% [*see Clinical Pharmacology (12.3)*].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

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