

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 H₁ 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*

1 INDICATIONS AND USAGE
1.1 Allergic Rhinitis

2 DOSAGE AND ADMINISTRATION
2.1 Seasonal Allergic Rhinitis
2.2 Perennial Allergic Rhinitis
2.3 Important Administration Instructions

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS
5.1 Activities Requiring Mental Alertness

6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Postmarketing Experience

7 DRUG INTERACTIONS
7.1 Central Nervous System Depressants
7.2 Erythromycin and Ketoconazole
7.3 Cimetidine

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL STUDIES
14.1 Seasonal Allergic Rhinitis
14.2 Perennial Allergic Rhinitis

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION
17.1 Activities Requiring Mental Alertness
17.2 Concurrent Use of Alcohol and Other Central Nervous System Depressants
17.3 Common Adverse Reactions
17.4 Priming
17.5 Keep Spray Out of Eyes
17.6 Keep Out of Children’s Reach

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

1 **FULL PRESCRIBING INFORMATION**

2 **1 INDICATIONS AND USAGE**

3 **1.1 Allergic Rhinitis**

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

7 **2 DOSAGE AND ADMINISTRATION**

8 **2.1 Seasonal Allergic Rhinitis**

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

12 **2.2 Perennial Allergic Rhinitis**

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

15 **2.3 Important Administration Instructions**

16 Administer ASTEPRO Nasal Spray by the intranasal route only.

17
18 Priming: Prime ASTEPRO Nasal Spray before initial use by releasing 6 sprays or
19 until a fine mist appears. When ASTEPRO Nasal Spray has not been used for 3 or more
20 days, reprime with 2 sprays or until a fine mist appears. Avoid spraying ASTEPRO Nasal
21 Spray into the eyes.

23 **3 DOSAGE FORMS AND STRENGTHS**

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

29 **4 CONTRAINDICATIONS**

30 None.

32 **5 WARNINGS AND PRECAUTIONS**

33 **5.1 Activities Requiring Mental Alertness**

34 In clinical trials, the occurrence of somnolence has been reported in some patients
35 taking ASTEPRO Nasal Spray [*see Adverse Reactions (6.1)*]. Patients should be
36 cautioned against engaging in hazardous occupations requiring complete mental alertness
37 and motor coordination such as operating machinery or driving a motor vehicle after
38 administration of ASTEPRO Nasal Spray. Concurrent use of ASTEPRO Nasal Spray
39 with alcohol or other central nervous system depressants should be avoided because
40 additional reductions in alertness and additional impairment of central nervous system
41 performance may occur [*see Drug Interactions (7.1)*].

43 **6 ADVERSE REACTIONS**

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

46 **6.1 Clinical Trials Experience**

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

50

51 *ASTEPRO Nasal Spray 0.1%*

52 The safety data described below reflect exposure to ASTEPRO Nasal Spray 0.1% in
 53 713 patients 12 years of age and older from 2 clinical trials of 2 weeks to 12 months
 54 duration. In a 2 week, double-blind, placebo-controlled, and active controlled (Astelin[®]
 55 Nasal Spray; azelastine hydrochloride) clinical trial, 285 patients (115 males and 170
 56 females) 12 years of age and older with seasonal allergic rhinitis were treated with
 57 ASTEPRO Nasal Spray 0.1% one or two sprays per nostril daily. In the 12 month open-
 58 label, active controlled (Astelin Nasal Spray) clinical trial, 428 patients (207 males and
 59 221 females) 12 years of age and older with perennial allergic rhinitis and/or nonallergic
 60 rhinitis were treated with ASTEPRO Nasal Spray 0.1% two sprays per nostril twice daily.
 61 The racial and ethnic distribution for the 2 clinical trials was 82% white, 8% black, 6%
 62 Hispanic, 3% Asian, and <1% other.

63

64 Adults and Adolescents 12 Years of Age and Older

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

73 Table 1 contains adverse reactions reported with frequencies greater than or equal
 74 to 2% and more frequently than placebo in patients treated with ASTEPRO Nasal Spray
 75 0.1% in the controlled clinical trial described above.

76

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%)

77

78 Long-Term (12 Month) Safety Trial:

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

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

91
 92 *ASTEPRO Nasal Spray 0.15%*

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

104
 105 Adults and Adolescents 12 Years of Age and Older

106 In the 7 placebo controlled clinical trials of 2 to 4 week duration, 2343 patients with
 107 seasonal allergic rhinitis and 540 patients with perennial allergic rhinitis were treated
 108 with two sprays per nostril of either ASTEPRO Nasal Spray 0.15% or placebo once or
 109 twice daily. Overall, adverse reactions were more common in the ASTEPRO Nasal Spray
 110 0.15% treatment groups (16-31%) than in the placebo groups (11-24%). Overall, less
 111 than 2% of patients discontinued due to adverse reactions and withdrawal due to adverse
 112 reactions was similar among the treatment groups.

113 Table 2 contains adverse reactions reported with frequencies greater than or equal to
 114 2% and more frequently than placebo in patients treated with ASTEPRO Nasal Spray
 115 0.15% in the seasonal and perennial allergic rhinitis controlled clinical trials.

116

Table 2. Adverse Reactions with $\geq 2\%$ 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%)

117
 118 In the above trials, somnolence was reported in <1% of patients treated with ASTEPRO
 119 Nasal Spray 0.15% (11 of 1544) or vehicle placebo (1 of 1339).

121 Long-Term (12 Month) Safety Trial:
122 In the 12 month, open-label, active-controlled, long-term safety trial, 466 patients (12
123 years of age and older) with perennial allergic rhinitis were treated with ASTEPRO Nasal
124 Spray 0.15% two sprays per nostril twice daily and 237 patients were treated with
125 mometasone nasal spray two sprays per nostril once daily. The most frequently reported
126 adverse reactions (>5%) with ASTEPRO Nasal Spray 0.15% were bitter taste, headache,
127 sinusitis, and epistaxis. Focused nasal examinations were performed and no nasal
128 ulcerations or septal perforations were observed. In each treatment group, approximately
129 3% of patients had mild epistaxis. No patients had reports of severe epistaxis. Fifty-four
130 patients (12%) treated with ASTEPRO Nasal Spray 0.15% and 17 patients (7%) treated
131 with mometasone nasal spray discontinued from the trial due to adverse events.
132

133 **6.2 Postmarketing Experience**

134 The following adverse reactions have been identified during the post approval use
135 of the Astelin brand of azelastine hydrochloride 0.1% nasal spray (total daily dose 0.55
136 mg to 1.1 mg). Because these reactions are reported voluntarily from a population of
137 uncertain size, it is not always possible to reliably estimate their frequency or establish a
138 causal relationship to drug exposure. Adverse reactions reported include the following:
139 anaphylactoid reaction, application site irritation, atrial fibrillation, blurred vision, chest
140 pain, confusion, dizziness, dyspnea, facial edema, hypertension, involuntary muscle
141 contractions, nervousness, palpitations, paresthesia, parosmia, paroxysmal sneezing,
142 pruritus, rash, disturbance or loss of sense of smell and/or taste, tachycardia, tolerance,
143 urinary retention, and xerophthalmia.
144

145 **7 DRUG INTERACTIONS**

146 **7.1 Central Nervous System Depressants**

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

150 **7.2 Erythromycin and Ketoconazole**

151 Interaction studies investigating the cardiac effects, as measured by the corrected
152 QT interval (QTc), of concomitantly administered oral azelastine hydrochloride and
153 erythromycin or ketoconazole were conducted. Oral erythromycin (500 mg three times
154 daily for 7 days) had no effect on azelastine pharmacokinetics or QTc based on analyses
155 of serial electrocardiograms. Ketoconazole (200 mg twice daily for 7 days) interfered
156 with the measurement of azelastine plasma concentrations on the analytic HPLC;
157 however, no effects on QTc were observed [*see Clinical Pharmacology (12.2) and*
158 *(12.3)*].

159 **7.3 Cimetidine**

160 Cimetidine (400 mg twice daily) increased the mean C_{max} and AUC of orally
161 administered azelastine hydrochloride (4 mg twice daily) by approximately 65%
162 [*see Clinical Pharmacology (12.3)*].
163

164 **8 USE IN SPECIFIC POPULATIONS**

165 **8.1 Pregnancy**

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.