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APPLICATION NUMBER:
202236Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use DYMISTA™ Nasal Spray safely and effectively. See full prescribing information for DYMISTA Nasal Spray.

DYMISTA (azelastine hydrochloride and fluticasone propionate) Nasal Spray

Initial U.S. Approval: 2012

INDICATIONS AND USAGE

Dymista Nasal Spray, containing an H₁-receptor antagonist and a corticosteroid, is indicated for the relief of symptoms of seasonal allergic rhinitis in patients 12 years of age and older who require treatment with both azelastine hydrochloride and fluticasone propionate for symptomatic relief. (1.1)

DOSAGE AND ADMINISTRATION

- For intranasal use only. (2.1)
- Recommended dose is 1 spray per nostril twice daily in adults and adolescents 12 years of age and older (2.1)
- Prime before initial use and when it has not been used for 14 or more days. (2.2)

DOSAGE FORMS AND STRENGTHS

Dymista Nasal Spray: 137 mcg of azelastine hydrochloride and 50 mcg of fluticasone propionate (137 mcg/50 mcg) in each 0.137 mL spray. (3)

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

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

- Epistaxis, nasal ulcerations, nasal septal perforation, impaired wound healing, *Candida albicans* infection. Monitor patients periodically for signs of adverse effects on the nasal mucosa. Avoid use in patients with recent nasal ulcers, nasal surgery, or nasal trauma. (5.2)
- Development of glaucoma or posterior subcapsular cataracts. Monitor patients closely with a change in vision or with a history of increased intraocular pressure, glaucoma, and/or cataracts. (5.3)
- Hypercorticism and adrenal suppression with very high dosages or at the regular dosage in susceptible individuals. If such changes occur, discontinue Dymista Nasal Spray slowly. (5.5)
- Potential reduction in growth velocity in children. Monitor growth routinely in pediatric patients receiving Dymista Nasal Spray. (5.7, 8.4)

ADVERSE REACTIONS

The most common adverse reactions (≥2% incidence) are: dysgeusia, epistaxis, and headache. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Meda Pharmaceuticals Inc. at 1-888-939-6478 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Potent inhibitors of cytochrome P450 (CYP) 3A4: May increase blood levels of fluticasone propionate.
- Ritanovir: Coadministration is not recommended. (5.6, 7.2)
- Other potent CYP3A4 inhibitors, such as ketoconazole: use caution with coadministration. (5.6, 7.2)

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on animal data, may cause fetal harm. (8.1)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 4/2012

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

1 FULL PRESCRIBING INFORMATION

2 **1 INDICATIONS AND USAGE**

3 Dymista Nasal Spray is indicated for the relief of symptoms of seasonal allergic rhinitis in
4 patients 12 years of age and older who require treatment with both azelastine hydrochloride and
5 fluticasone propionate for symptomatic relief.

6 **2 DOSAGE AND ADMINISTRATION**

7 **2.1 Dosing Information**

8 The recommended dose of Dymista Nasal Spray, 137 mcg/50 mcg, is 1 spray per nostril twice
9 daily for seasonal allergic rhinitis. Each spray contains 137 mcg of azelastine hydrochloride and
10 50 mcg of fluticasone propionate (137 mcg/50 mcg).

11

12 Administer Dymista Nasal Spray by the intranasal route only.

13

14 **2.2 Important Administration Instructions**

15 Shake the bottle gently before each use.

16 Priming: Prime Dymista Nasal Spray before initial use by releasing 6 sprays or until a fine mist
17 appears. When Dymista Nasal Spray has not been used for 14 or more days, reprime with 1 spray
18 or until a fine mist appears. Avoid spraying Dymista Nasal Spray into the eyes. If sprayed in the
19 eyes, flush eyes with water for at least 10 minutes.

20 **3 DOSAGE FORMS AND STRENGTHS**

21 Dymista is a nasal spray suspension. Each spray delivers a volume of 0.137 mL suspension
22 containing 137 mcg of azelastine hydrochloride and 50 mcg of fluticasone propionate (137
23 mcg/50 mcg).

24 **4 CONTRAINDICATIONS**

25 None.

26 **5 WARNINGS AND PRECAUTIONS**

27 **5.1 Somnolence**

28 In clinical trials, the occurrence of somnolence has been reported in some patients (6 of 853
29 patients) taking Dymista Nasal Spray [*see Adverse Reactions (6.1)*]. Patients should be cautioned
30 against engaging in hazardous occupations requiring complete mental alertness and motor

31 coordination such as operating machinery or driving a motor vehicle after administration of
32 Dymista Nasal Spray. Concurrent use of Dymista Nasal Spray with alcohol or other central
33 nervous system depressants should be avoided because additional reductions in alertness and
34 additional impairment of central nervous system performance may occur [*see Drug Interactions*
35 (7.1)].

36 **5.2 Local Nasal Effects**

37 In clinical trials of 2 to 52 weeks' duration, epistaxis was observed more frequently in patients
38 treated with Dymista Nasal Spray than those who received placebo [*see Adverse Reactions (6)*].

39 Instances of nasal ulceration and nasal septal perforation have been reported in patients
40 following the intranasal application of corticosteroids. There were no instances of nasal
41 ulceration or nasal septal perforation observed in clinical trials with Dymista Nasal Spray.

42 Because of the inhibitory effect of corticosteroids on wound healing, patients who have
43 experienced recent nasal ulcers, nasal surgery, or nasal trauma should not use Dymista Nasal
44 Spray until healing has occurred.

45 In clinical trials with fluticasone propionate administered intranasally, the development of
46 localized infections of the nose and pharynx with *Candida albicans* has occurred. When such an
47 infection develops, it may require treatment with appropriate local therapy and discontinuation of
48 treatment with Dymista Nasal Spray. Patients using Dymista Nasal Spray over several months
49 or longer should be examined periodically for evidence of *Candida* infection or other signs of
50 adverse effects on the nasal mucosa.

51 **5.3 Glaucoma and Cataracts**

52 Nasal and inhaled corticosteroids may result in the development of glaucoma and/or cataracts.
53 Therefore, close monitoring is warranted in patients with a change in vision or with a history of
54 increased intraocular pressure, glaucoma, and/or cataracts.

55 Glaucoma and cataract formation were evaluated with intraocular pressure measurements and slit
56 lamp examinations in a controlled 12-month study in 612 adolescent and adult patients aged 12
57 years and older with perennial allergic or vasomotor rhinitis (VMR). Of the 612 patients enrolled
58 in the study, 405 were randomized to receive Dymista Nasal Spray (1 spray per nostril twice
59 daily) and 207 were randomized to receive fluticasone propionate nasal spray (2 sprays per
60 nostril once daily). In the Dymista Nasal Spray group, one patient had increased intraocular
61 pressure at month 6. In addition, three patients had evidence of posterior subcapsular cataract at
62 month 6 and one at month 12 (end of treatment). In the fluticasone propionate group, three
63 patients had evidence of posterior subcapsular cataract at month 12 (end of treatment).

64 **5.4 Immunosuppression**

65 Persons who are using drugs, such as corticosteroids, that suppress the immune system are more
66 susceptible to infections than healthy individuals. Chickenpox and measles, for example, can
67 have a more serious or even fatal course in susceptible children or adults using corticosteroids. In
68 children or adults who have not had these diseases or been properly immunized, particular care
69 should be taken to avoid exposure. How the dose, route, and duration of corticosteroid
70 administration affect the risk of developing a disseminated infection is not known. The

71 contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not
72 known. If exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG)
73 may be indicated. If exposed to measles, prophylaxis with pooled intramuscular immunoglobulin
74 (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing
75 information.) If chickenpox develops, treatment with antiviral agents may be considered.

76 Corticosteroids should be used with caution, if at all, in patients with active or quiescent
77 tuberculous infections of the respiratory tract; untreated local or systemic fungal or bacterial
78 infections; systemic viral or parasitic infections; or ocular herpes simplex because of the
79 potential for worsening of these infections.

80 **5.5 Hypothalamic-Pituitary-Adrenal (HPA) Axis Effects**

81 When intranasal steroids are used at higher than recommended dosages or in susceptible
82 individuals at recommended dosages, systemic corticosteroid effects such as hypercorticism and
83 adrenal suppression may appear. If such changes occur, the dosage of Dymista Nasal Spray
84 should be discontinued slowly, consistent with accepted procedures for discontinuing oral
85 corticosteroid therapy. The concomitant use of intranasal corticosteroids with other inhaled
86 corticosteroids could increase the risk of signs or symptoms of hypercorticism and/or
87 suppression of the HPA axis.

88 The replacement of a systemic corticosteroid with a topical corticosteroid can be accompanied
89 by signs of adrenal insufficiency, and in addition some patients may experience symptoms of
90 withdrawal, e.g., joint and/or muscular pain, lassitude, and depression. Patients previously
91 treated for prolonged periods with systemic corticosteroids and transferred to topical
92 corticosteroids should be carefully monitored for acute adrenal insufficiency in response to
93 stress. In those patients who have asthma or other clinical conditions requiring long-term
94 systemic corticosteroid treatment, too rapid a decrease in systemic corticosteroids may cause a
95 severe exacerbation of their symptoms.

96 **5.6 Use of Cytochrome P450 3A4 Inhibitors**

97 Ritonavir and other strong cytochrome P450 3A4 (CYP3A4) inhibitors can significantly increase
98 plasma fluticasone propionate exposure, resulting in significantly reduced serum cortisol
99 concentrations [*see Drug Interactions (7.2) and Clinical Pharmacology (12.3)*]. During
100 postmarketing use, there have been reports of clinically significant drug interactions in patients
101 receiving fluticasone propionate and ritonavir, resulting in systemic corticosteroid effects
102 including Cushing syndrome and adrenal suppression. Therefore, coadministration of Dymista
103 Nasal Spray and ritonavir is not recommended unless the potential benefit to the patient
104 outweighs the risk of systemic corticosteroid side effects.

105 Use caution with the coadministration of Dymista Nasal Spray and other potent CYP3A4
106 inhibitors, such as ketoconazole [*see Drug Interactions (7.2) and Clinical Pharmacology (12.3)*].

107 **5.7 Effect on Growth**

108 Corticosteroids may cause a reduction in growth velocity when administered to pediatric
109 patients. Monitor the growth routinely of pediatric patients receiving Dymista Nasal Spray [*see*
110 *Use in Specific Populations (8.4)*].

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