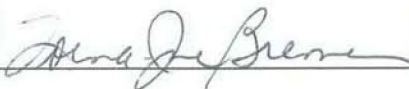


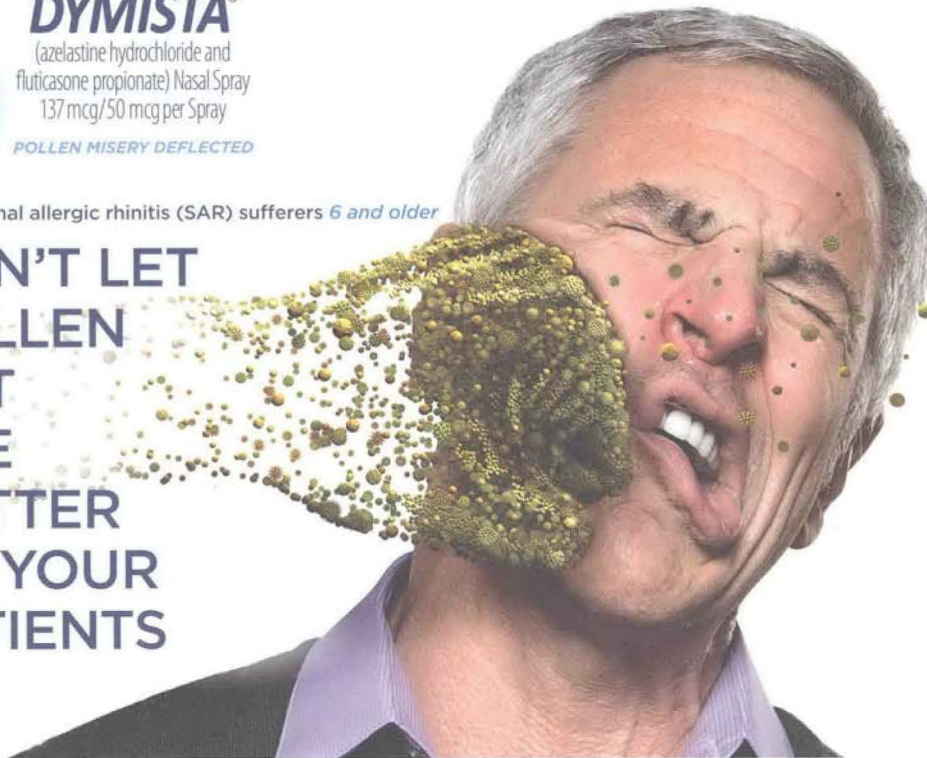
11. Typed Name and Title of Responsible Official or Agent Lorna-Jane Bremer, Senior Director Regulatory Affairs	12. Signature of Responsible Official or Agent  <div data-bbox="1144 185 1226 229" style="border: 1px solid black; padding: 2px; display: inline-block;">Sign</div>	13. Date 06/16/2015
14. For CBER Products Only (Check one) <div style="display: flex; justify-content: space-around; margin-top: 5px;"> <input type="checkbox"/> Draft <input type="checkbox"/> Final </div>		
<p style="text-align: center;">This section applies only to requirements of the Paperwork Reduction Act of 1995.</p> <p style="text-align: center;">*DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.*</p> <p>The burden time for this collection of information is estimated to average 2 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:</p> <p style="text-align: center;"> Department of Health and Human Services Food and Drug Administration Office of Chief Information Officer Paperwork Reduction Act (PRA) Staff PRASaff@fda.hhs.gov </p> <p style="text-align: center;"><i>"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."</i></p>		



DYMISTA[®]
(azelastine hydrochloride and
fluticasone propionate) Nasal Spray
137 mcg/50 mcg per Spray
POLLEN MISERY DEFLECTED

For seasonal allergic rhinitis (SAR) sufferers **6 and older**

**DON'T LET
POLLEN
GET
THE
BETTER
OF YOUR
PATIENTS**



Only Dymista offers fast relief^a and inflammation control—with every dose^{1,2}

^aAs demonstrated in patients 12 and older, fast relief is defined as the first timepoint (30 minutes) at which Dymista was significantly superior to placebo in the mean change from baseline in instantaneous total nasal symptom score (ITNSS) and was sustained thereafter.¹

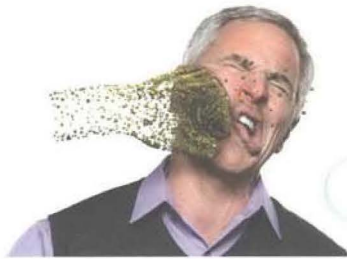
Indications

DYMISTA contains an H1-receptor antagonist and a corticosteroid, and is indicated for the relief of symptoms of seasonal allergic rhinitis in patients 6 years of age and older who require treatment with both azelastine hydrochloride and fluticasone propionate for symptomatic relief.

Important Safety Information

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

Please see additional Important Safety Information throughout and Full Prescribing Information in pocket.



3 pivotal clinical studies of total nasal symptom scores showed

RAPID RELIEF

BECAUSE PATIENTS HAVE WAITED LONG ENOUGH

Onset of nasal
symptom relief
as fast as

30 minutes¹
vs placebo ($P < .05$)

Onset was defined as the first timepoint at which Dymista was significantly superior to placebo in the mean change from baseline in iTNSS and was sustained thereafter in patients $\geq 12^{1,a}$

► In an independent survey, 85% of patients identified rapid relief of symptoms as one of the most important attributes of allergic rhinitis treatment²

^a iTNSS is calculated as the sum of the patients' scoring of the 4 individual nasal symptoms (rhinorrhea, congestion, sneezing, and itching) on a 0 to 3 categorical severity scale (0=absent, 1=mild, 2=moderate, 3=severe).¹

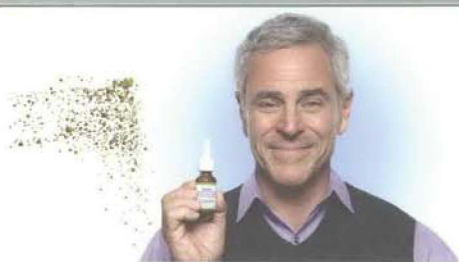
Important Safety Information continued

- 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.
- Potential worsening of existing tuberculosis; fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex. More serious or even fatal course of chickenpox or measles in susceptible patients. Use caution in patients with the above because of the potential for worsening of these infections.
- Hypercorticism and adrenal suppression with very high dosages or at the regular dosage in susceptible individuals. If such changes occur, discontinue DYMISTA slowly.

Please see additional Important Safety Information throughout and Full Prescribing Information in pocket.

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2



DYMISTA®
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fluticasone propionate) Nasal Spray
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POLLEN MISERY DEFLECTED

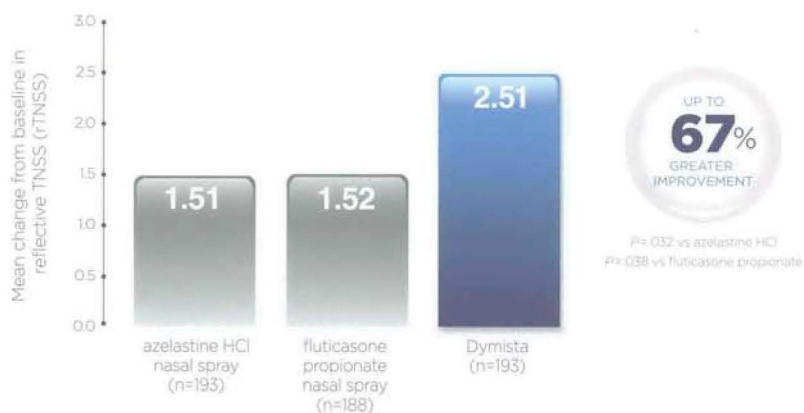
SUPERIOR EFFICACY

VS AZELASTINE HCL OR

FLUTICASONE PROPIONATE COMPARATORS

Dymista demonstrated significantly greater improvement in reflective total nasal symptom relief in patients ≥ 12 .^{1,4}

MAGNITUDE OF NASAL SYMPTOM RELIEF



Data shown are from pivotal study MP 4004. Across all 3 pivotal clinical trials, Dymista provided a significant improvement in rTNSS with Dymista, ranging from 43% to 67% relative to azelastine HCl or fluticasone propionate comparators, as presented in the Full Prescribing Information.^{1,4}

Change from baseline in the placebo-subtracted mean rTNSS for each day (maximum score 24), averaged over the 14-day study period. Percent difference represents the improvement in rTNSS with Dymista relative to azelastine HCl or fluticasone propionate comparators. **The azelastine HCl and fluticasone propionate comparators were delivered via the same device and vehicle as Dymista and are not commercially available.**^{1,4}

3



A supportive SAR trial showed

SIGNIFICANT IMPROVEMENT VS PRODUCTS YOUR PATIENTS MAY HAVE TRIED

Dymista demonstrated significantly greater improvement in total nasal symptom relief vs Astelin® (azelastine HCl) or generic Flonase® (fluticasone propionate) in patients ≥ 12 .^{2,4}

MAGNITUDE OF NASAL SYMPTOM RELIEF



Change from baseline in the placebo-subtracted mean TNSS for each day (maximum score 24), averaged over the 14-day study period.²

Percent difference represents the improvement in TNSS with Dymista relative to commercially available generic Flonase® (fluticasone propionate) comparator.^{2,4}

► The most common adverse events with Dymista in this trial were dysgeusia (72%), epistaxis (3.9%), and headache (2.6%).²

Important Safety Information continued

- Potential reduction in growth velocity in children. Monitor growth routinely in pediatric patients receiving DYMISTA.

Please see additional Important Safety Information throughout and Full Prescribing Information in pocket.

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4



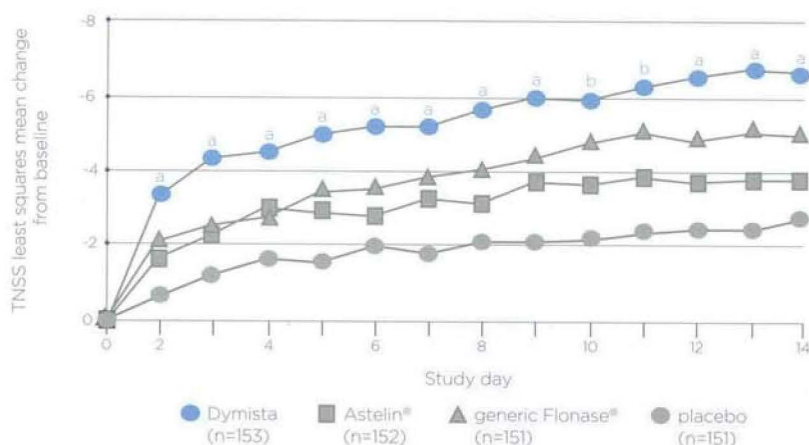
DYMISTA®
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POLLEN MISERY DEFLECTED

A supportive SAR trial showed

SUSTAINED IMPROVEMENT VS PRODUCTS YOUR PATIENTS MAY HAVE TRIED

Dymista demonstrated significantly greater improvement in total nasal symptom relief vs active comparators and placebo over time ($P < .001$) in patients ≥ 12 .^{2,4}

SUSTAINED IMPROVEMENT OVER 2 WEEKS



² $P < .01$ vs Astelin®, generic Flonase®, and placebo.³

³ $P < .01$ vs Astelin® and placebo.²

► Significant separation was demonstrated by the Dymista group as early as Day 2

Important Safety Information continued

- Potent inhibitors of cytochrome P450 (CYP) 3A4: May increase blood levels of fluticasone propionate.
- Ritonavir: Coadministration is not recommended.
- Other potent CYP3A4 inhibitors, such as ketoconazole: use caution with coadministration.
- The most common adverse reactions reactions ($\geq 2\%$ incidence) are: dysgeusia, epistaxis, and headache.

5



SAFETY AND TOLERABILITY

DYMISTA HAS BEEN WIDELY STUDIED IN >4000 PATIENTS

Safety/efficacy pivotal trials in rhinitis, including SAR:
In each of the three 2-week pivotal trials, incidence and types of adverse reactions were comparable in all treatment groups (N=3411)¹

TAKE
A CLOSER
LOOK

Adverse reactions occurring with
≥2% incidence and more frequently
than with placebo¹

	Dymista	azelastine HCl ^a	fluticasone propionate ^a	placebo
Overall incidence	16%	15%	13%	12%
Dysgeusia	4%	5%	1%	<1%
Epistaxis	2%	2%	2%	2%
Headache	2%	2%	2%	1%

^aThe azelastine HCl and fluticasone propionate comparators were delivered via the same device and vehicle as Dymista and are not commercially available.¹

Long-term safety trial: In a separate, 12-month, open-label safety trial (N=611), the overall rate of any adverse reaction was 47% with Dymista and 44% with fluticasone propionate^{1,2}

► Of patients treated with Dymista:

- None had severe epistaxis, 2% had mild epistaxis, and <1% had moderate epistaxis
- No nasal ulcerations or septal perforations were observed

► In both treatment groups, 3% of patients discontinued use because of adverse reactions

¹As listed in the Full Prescribing Information, this trial was an open-label, active-controlled study in which 404 patients (12 years of age and older) with chronic allergic or nonallergic vasomotor rhinitis were treated with Dymista 1 spray per nostril twice daily, and 207 patients were treated with fluticasone propionate 2 sprays per nostril once daily.¹

Please see additional Important Safety Information throughout
and Full Prescribing Information in pocket.

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6



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POLLEN MISERY DEFLECTED

SAFETY AND TOLERABILITY IN CHILDREN 6-11 YEARS OF AGE

Safety results from a double-blind, placebo-controlled clinical trial in children with SAR treated with Dymista for 2 weeks (N=304)¹

Adverse reactions occurring with $\geq 2\%$ incidence and more frequently than with placebo¹

	Dymista	placebo
Overall incidence	16%	12%
Dysgeusia	4%	0%
Epistaxis	4%	3%

In a separate, 3-month, open-label safety trial (N=353) of children aged 6 to 11 years¹

- ▶ No nasal ulcerations or septal perforations were observed
- ▶ 2% of patients in the Dymista group and 3% in the fluticasone group discontinued use because of adverse events
- ▶ There were two reports of somnolence, one severe, among children taking Dymista

1 spray per nostril, twice daily¹

Important Safety Information continued

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



For seasonal allergic rhinitis sufferers 6 and older

DON'T LET POLLEN GET THE BETTER OF YOUR PATIENTS



Only Dymista offers fast relief^a and inflammation control—with every dose^{1,2}

^aAs demonstrated in patients 12 and older, fast relief is defined as the first timepoint (30 minutes) at which Dymista was significantly superior to placebo in the mean change from baseline in instantaneous total nasal symptom score (iTNSS) and was sustained thereafter.¹

► 1 spray per nostril, twice daily¹

► 30 minutes fast—onset^a in as soon as a half hour vs placebo¹

► Up to 67% greater improvement than azelastine HCl or fluticasone propionate comparators^{1,4}

Across all 3 pivotal clinical trials, involving patients 12 and older, Dymista provided a significant improvement in placebo-subtracted iTNSS, ranging from 43% to 67% greater than that of azelastine HCl or fluticasone propionate, as presented in the Full Prescribing Information. iTNSS is calculated as the sum of the patients' scoring of the 4 individual nasal symptoms (rhinorrhea, congestion, sneezing, and itching) on a 0 to 3 categorical severity scale (0-absent, 1-mild, 2-moderate, 3-severe). Daily symptom scores were averaged over the 14-day study period. The comparators were delivered via the same device and vehicle as Dymista and are not commercially available.^{1,4}

► 90% greater improvement than generic Flonase[®] (fluticasone propionate)^{2,4}

In a supportive study, involving patients 12 and older, Dymista provided a significant improvement in placebo-subtracted iTNSS vs generic Flonase[®] (fluticasone propionate). Daily symptom scores were averaged over the 14-day study period.²

Dymista: Low spray volume at the maximum recommended adult dose^{1,5,6}

Product	Astelín [®] (azelastine HCl) ^c	generic Flonase [®] (fluticasone propionate) ^c	Astelín [®] + (azelastine HCl)	generic Flonase [®] (fluticasone propionate)	Dymista
Volume	548 µL	400 µL	948 µL		274 µL

There is no demonstrated clinical benefit regarding spray volume.

^cAt maximum recommended adult dose of 2 sprays per nostril.

Important Safety Information continued

- 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.
- 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.

Please see additional Important Safety Information throughout and Full Prescribing Information in pocket.

All trademarks are the property of their respective owners.

References: 1. Dymista [package insert]. Somerset, NJ: Meda Pharmaceuticals Inc; 2015. 2. Hampel FC, Ratner PH, Van Bavel J, et al. Double-blind, placebo-controlled study of azelastine and fluticasone in a single nasal spray delivery device. *Ann Allergy Asthma Immunol*. 2010;105(2):168-173. 3. Marple BF, Fornadley JA, Patel AA, et al. American Academy of Otolaryngic Allergy Working Group on Allergic Rhinitis. Keys to successful management of patients with allergic rhinitis: focus on patient confidence, compliance, and satisfaction. *Otolaryngol Head Neck Surg*. 2007;136(5)(suppl):S107-S124. 4. Data on File. Meda Pharmaceuticals Inc. 5. Astelín [package insert]. Somerset, NJ: Meda Pharmaceuticals Inc; 2014. 6. Flonase [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2015.

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