CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-371s000

OTHER REVIEW(S)

Division of Pulmonary and Allergy Products

REGULATORY PROJECT MANAGER REVIEW

Application Number: 22-371
22-203/S-003

Name of Drug: Astepro™ (azelastine hydrochloride) Nasal Spray

Applicant: MEDA Pharmaceuticals

Material Reviewed:

Submission Date: August 28, 2009
Receipt Date: August 31, 2009

Background and Summary

MEDA Pharmaceuticals submitted NDA 22-371 as a 505(b)(1) application for Astepro (azelastine hydrochloride) Nasal Spray 0.15% for the relief of symptoms of seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR) in patients 12 years of age and older.

NDA 22-203/S-003 is a prior approval labeling supplement for Astepro(azelastine hydrochloride) Nasal Spray 0.10% which provides for revisions to the package insert and the carton/container labeling to harmonize with the agreed upon labeling for NDA 22-371. With approval of NDA 22-371, the labeling will be merged for both NDA applications. NDA 22-371 will be administratively closed and all future submissions will be addressed to NDA 22-203.

Review

The revisions to the package insert and the carton/container labeling were reviewed by the assigned review team for both applications. CMC comments for the carton/container were relayed to MEDA in a facsimile dated August 8, 2009. MEDA incorporated the FDA's proposed changes to the carton/container in their submission dated August 17, 2009. CMC found the amended carton/container labeling revisions acceptable.

The most recent Agency comments for the package insert were relayed to MEDA in a facsimile dated August 26, 2009. MEDA submitted revised labeling to incorporate Agency comments in a facsimile dated August 27, 2009, and submitted the labeling to both applications. Dr. Sally Seymour, CDTL for this application, found numerical errors and the company was notified via telephone on August 28, 2009. MEDA subsequently submitted revised labeling dated August 28, 2009. The August 28, 2009, labeling is acceptable by the review team.

I compared the draft package insert labeling August 28, 2009, to the agreed upon labeling outlined in our August 26, 2009, facsimile. The draft labeling submitted was identical to our labeling outlined in our August 26, 2009, facsimile except for those numerical adjustments requested by the CDTL.

Conclusions

The package insert labeling dated August 28, 2009, should be approved for both applications.

Colette Jackson
Regulatory Health Project Manager

Supervisory Comment/Concurrence:

Sandy Barnes
Chief, Project Management Staff

Drafted: CCJ/ August 27, 2009
Revised/Initialed: CCJ/ August 30, 2009
Finalized: CCJ/ August 30, 2009
Filename: 22371 and 22203 s003 PM Labeling Review

CSO LABELING REVIEW

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/s/

COLETTE C JACKSON
08/31/2009

MIRANDA B RAGGIO on behalf of SANDRA L BARNES
08/31/2009

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	August 4, 2009
To:	Badrul Chowdhury, MD, Director Division of Pulmonary and Allergy Products
Through:	Kellie Taylor, PharmD, MPH, Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis
From:	Zachary Oleszczuk, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Label and Labeling Review
Drug Name(s):	Astepro (Azelastine Hydrochloride) Nasal Spray 0.1% and 0.15%
Application Type/Number:	NDA 22-203 and 22-371
Applicant/sponsor:	MEDA Pharmaceuticals
OSE RCM #:	2009-1348

CONTENTS

1 INTRODUCTION

This review was written in response to a request from the Division of Pulmonary and Allergy Products (DPAP) for assessment of the labels and labeling for NDA's 22-203 and 22-371 to identify areas that could lead to medication errors. MEDA Pharmaceuticals submitted amendment 0017, for NDA 22-371, dated July 15, 2009, for the labels and labeling for the product Astepro (Azelastine Hydrochloride) Nasal Spray 0.15%. Additionally, MEDA Pharmaceuticals stated in the cover letter of amendment 0017 of NDA 22-371, that the Applicant will submit a prior approval supplement containing revised labels and labeling for NDA 22-203, Astepro 0.1%.

2 MATERIALS REVIEWED

For this product the Applicant submitted labels and labeling on July 15, 2009 (see Appendices A and B).

Using Failure Mode and Effects Analysis,[1] DMEPA evaluated the container labels, carton labeling and insert labeling to identify vulnerabilities that could lead to medication errors. Additionally, since Astepro 0.1% is currently marketed DMEPA conducted a search of the FDA Adverse Event Reporting System (AERS) database to identify any errors that may be occurring with the currently marketed label and labeling.

2.1 AERS DATABASE

DMEPA searched the AERS database on July 22, 2009 using the MedRA High Level Group Term (HLGT) "Medication Errors" and Preferred Term (PT) "Pharmaceutical product complaint" as search criteria for Reactions. The search criteria used for Products were active ingredients "Aze%", trade name "Aste%" and verbatim substance search "Aze%" and "Aste%". Date limitations were used from April 1, 2009 to July 22, 2009, since a previous review dated May 5, 2009, (see OSE Review 2008-1414) completed an AERS search from October 25, 2008, through April 1, 2008 which did not identify any cases relevant to this review.

The AERS search identified one case that was relevant to this review. A male patient confused Astepro 0.1% nasal spray with an Albuterol inhaler. The patient administered Astepro by the oral route. After realizing the mistake the patient took a dose of Spiriva and 2 doses of Albuterol. One of the doses of Albuterol was taken in error as stated in the case. Following the two doses of Albuterol the patient went to the emergency room for increased hart rate. The report stated that the patient had recovered form the event. The reporter did not state a cause for the confusion or the error.

[1] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

Although the patient reportedly suffered an adverse event in this case, it is unclear whether the adverse event is attributable to the error or the other medications administered. A known side effect of Albuterol overdose is increased heart rate. This is the only case that reported confusion between Astepro and another product. The case did not report what caused the patient to confuse Astepro for Albuterol. However, we investigated the carton labeling and container label submitted for Astepro 0.1% and Astepro 0.15% to see if improvements could be made to prevent similar errors.

The label and labeling states the intended route of administration (the carton labeling clearly states "Nasal Spray" and the container labels state "FOR INTRANASAL USE ONLY") which should help mitigate the risk of administering Astepro via the wrong route. However, the container statement is not bolded and is located directly above the statement (b) (4) which is bolded. Revising the container labels so that the intended route of administration is more prominent should help to minimize the risk of administering the Astepro products by the wrong route in the future.

3 RECOMMENDATIONS

The assessment of the proposed labels and labeling indicates that the presentation of information on the labels and labeling could be improved to help minimize confusion that could lead to medication errors. We provide recommendations below that aim at reducing the risk of medication errors. We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention and Analysis on any communication to the Applicant with regard to this review. If you have further questions or need clarifications, please contact Sean Bradley, OSE Project Manager, at 301-796-1332.

We request the following recommendations be communicated to the Applicant prior to approval.

3.1 COMMENTS TO THE APPLICANT

A. Container Labels and Carton Labeling

1. Ensure that the established name is half the size and the appropriate prominence compared to the proprietary name per 21 CFR 201.10 (g)(2).

B. Container Labels

1. The same color scheme of a blue background and white font are used for the proposed strength and the currently marketed strength. This could lead to selection confusion between the two products if the products are not stored within the carton and in a similar location on the pharmacy shelf. In order to increase the visual difference between the two strengths we request that you revise the color of the blue box on the container label to better differentiate the two Astepro products.

2. Delete the statement [redacted]" or provide the rational for inclusion of the statement on the container. Negative statements such as [redacted] may actually have the opposite intended effect and have inadvertently encouraged wrong routes of administration due to the reader's focus on the route of administration and the potential for overlooking the negative words 'not' or 'do not'. To ensure that Astepro is administered via the appropriate route, increase the prominence of the statement "FOR INTRANASAL USE" by bolding this statement and remove the statement [redacted]

C. Insert Labeling

1. Both the currently marketed Astepro 0.1% and the proposed Astepro 0.15% have an overlap in the volume dispensed per each spray (0.137 mL per spray). Additionally, the volume dispensed per spray of the proposed Astepro 0.15% product (**0.137 mL**) numerically overlaps with the strength of the currently marketed Astepro 0.1% product (**0.137 mg**). Although the units are different (mL vs. mg), this numerical overlap may cause confusion if the volume dispensed per spray is interpreted as the dose and the units are overlooked. To avoid confusion, delete the references to the volume [redacted] in the Higlights section under "DOSAGE FORMS AND STRENGTHS". The statements should read:

   ASTEPRO Nasal Spray 0.1%: 137 mcg of azelastine hydrochloride in each spray (3).

   ASTEPRO Nasal Spray 0.15%: 205.5 mcg of azelastine hydrochloride in each spray (3).

4 REFERENCES

1. Adverse Events Reporting System (AERS)

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufactures that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential post-marketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

2. Reviews

OSE Review #2008-1414 Proprietary Astepro (b) (4) 205.5 mcg) Label and Labeling Review, Oleszczuk, Z; May 5, 2009.

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/s/

KELLIE A TAYLOR
08/04/2009

DENISE P TOYER
08/04/2009

CAROL A HOLQUIST
08/04/2009

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	May 05, 2009
To:	Badrul Chowdhury, MD, Director Division of Pulmonary and Allergy Products
Through:	Kellie Taylor, PharmD, MPH, Team Leader Denise P. Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis
From:	Zachary Oleszczuk, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Label and Labeling Review
Drug Name(s):	Astepro (b) (4) (Azelastine Hydrochloride) Nasal Spray 205.5 mcg/actuation
Application Type/Number:	NDA 22-371
Applicant/sponsor:	MEDA Pharmaceuticals, Inc.
OSE RCM #:	2008-1414

EXECUTIVE SUMMARY

This review was written in response to the label and labeling submission from MEDA Pharmaceuticals, dated February 09, 2009 for the product, Astepro 0.15% (NDA #22-371).

Astepro (Azelastine Hydrochloride) Nasal Spray is currently marketed as a product identical to Astepro 0.15% with the exception of strength (0.1 % vs. 0.15 %). Astepro 0.15% also has an additional proposed indication of perennial allergic rhinitis for adults and adolescents 12 years of age or older. DMEPA evaluated the labels and labeling using Failure Mode and Effects Analysis,[1] and applying lessons learned from postmarketing experience with Astepro to identify vulnerabilities that could lead to medication errors.

Our findings indicate that revisions could be made to the presentation of strength to more clearly differentiate this product from the currently marketed Astepro. Additionally, changing the color scheme of the container labels and carton labeling may also help to differentiate the products. Our recommendations are provided in Section 2.

1 MATERIALS REVIEWED

Container labels and carton labeling submitted as part of the February 09, 2009 proprietary name submission (Appendix A and B). Additionally, the package insert labeling was submitted on April 10, 2009 (no image).

Since Astepro is identical to Astepro 0.15% with the exception of strength and the lack of the perennial allergic rhinitis indication and Astepro is currently marketed, DMEPA conducted a search of the Adverse Event Reporting System (AERS) database to determine if there are any medication errors associated with label or labeling confusion with the currently marketed Astepro that may be indicative of potential label or labeling confusion with Astepro 0.15%.

DMEPA searched the AERS database on April 1, 2009 using the MedRA High Level Group Term (HLGT) "Medication Errors" and Preferred Term (PT) "Pharmaceutical product complaint" as search criteria for Reactions. The search criteria used for Products were active ingredients "Aze%", trade name "Aste%" and verbatim substance search "Aze%" and "Aste%". Date limitations were used from October 25, 2008, to April 1, 2008, since Astepro was approved on October 25, 2008.

The search yielded three cases, in which none were relevant to this review.

[1] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

2 RECOMMENDATIONS

2.1 COMMENTS TO THE DIVISION

Because we are recommending in OSE Review #2009-304, that NDA 22-371 be managed under the proprietary name "Astepro" it is important to differentiate the proposed labels from the currently marketed labels. Additionally, revisions to the currently marketed product would also be needed. We request that the Applicant submit a supplement to NDA 22-203.

1. Revise the presentation of the strength to be a percentage (0.1%). Presenting the strength as a percentage would be easier for prescribers to order and to differentiate the products. Additionally, place the statement "137 mcg per spray" in parenthesis. (For example)

   Tradename
   (azelastine HCL)
   Nasal Spray 0.1%
   (137 mcg per spray)

2. Revise the net quantity statement, (b) (4) on the side panel of the carton labeling for NDA 22-203 to state "XX Metered Sprays".

3. Delete the statement, (b) (4) on the principal display panel of the container label for NDA 22-203.

2.2 COMMENTS TO THE APPLICANT

A. General Comments on container labels and carton labeling

1. Remove the Abbreviation (b) (4) from the label and labeling. We requested you manage this proposed product and the currently marketed Astepro product under the same proprietary name "Astepro" and differentiate the two products by their strengths.

2. The proposed azelastine product and the currently marketed Astepro product only differ in respect to strength. Thus, it is important to highlight this difference so selection errors and prescribing errors are minimized upon launch of this product. In order to accomplish this goal we request that the strength be expressed in terms of a percentage. Presenting the strength as a percentage would be easier for prescribers to order and to differentiate the products (e.g. 0.15%). Additionally, place the statement "205.5 mcg per spray" in parenthesis as presented below:

   Tradename
   (azelastine HCL)
   Nasal Spray 0.15%
   (205.5 mcg per spray)

3. The proposed name and strength appear in a dark blue box. This is similar to the currently marketed '0.1% (137 mcg)' presentation of the name and strength. In order to increase the visual difference between the 2 strengths we request that you revise the color of the box on the container label and carton labeling so that it does not overlap with blue colored box on the container label or carton labeling for the currently marketed Astepro.

B. Container Labels (0.15% (205.5 mcg) 4 mL, 17 mL, and 30 mL bottles)

1. Both the currently marketed product and the proposed product have an overlap in the volume dispensed per each spray (0.137 mL per spray). Additionally, the volume dispensed per spray of the proposed product overlaps with the strength of the currently marketed product (0.137 mL vs. 0.137 mg). This overlap may cause confusion if the volume dispensed per spray is interpreted as the dose. Delete the statement, (b) (4) on the principal display panel of the container label.

2. Delete the statement (b) (4) or provide the rational for inclusion of the statement on the container.

C. Carton labeling (0.15% (205.5 mcg) 4 mL, 17 mL, and 30 mL bottles)

The net quantity statement (b) (4) on the side panel may be misinterpreted to mean that each spray delivers XX metered units per spray. Thus we request that you delete the word (b) (4) from the statement so that the statement reads "XX Metered Sprays".

D. Insert Labeling

Both the currently marketed product and the proposed product have an overlap in the volume dispensed per each spray (0.137 mL per spray). Additionally, the volume dispensed per spray of the proposed product (0.137 mL) overlaps with the strength of the currently marketed product (0.137 mg). Although the units of each quantity are different, this numerical overlap may cause confusion if the volume dispensed per spray is interpreted as the dose and the units are overlooked. Revise the "DOSAGE FORMS AND STRENGTHS" in the Highlights section to remove both instances of the statement (b) (4)

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/s/

Zachary A Oleszczuk
5/5/2009 12:34:24 PM
DRUG SAFETY OFFICE REVIEWER

Kellie Taylor
5/5/2009 01:46:51 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
5/5/2009 01:55:59 PM
DRUG SAFETY OFFICE REVIEWER

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	April 29, 2009
To:	Badrul Chowdhury, M.D. Division Director
	Division of Pulmonary and Allergy Products
Through:	Jodi Duckhorn, MA, Team Leader
	Division of Risk Management
From:	LaShawn Griffiths, MSHS-PH, BSN, RN
	Patient Product Information Reviewer
	Division of Risk Management
Subject:	DRISK Review of Patient Labeling (Patient Package Insert) and (Patient Instructions for Use)
Drug Name(s):	TRADENAME (azelastine hydrochloride) Nasal Spray
Application Type/Number:	NDA 22-371
Applicant/sponsor:	Meda Pharmaceuticals
OSE RCM #:	2008-1414

1 INTRODUCTION

Meda Pharnaceuticals submitted a New Drug Application (NDA) 22-371 for TRADENAME (azelastine hydrochloride) (0.15%) nasal spray on August 1, 2008. The submission includes proposed Professional Information (PI) in PLR format, with Patient Labeling Information (Patient Package Insert) and Instructions for Use (IFU). TRADENAME (azelastine hydrochloride) nasal spray is indicated for the relief of symtptoms associated with allergic rhinitis (seasonal and perennial) in patients 12 years of age and older.

The Division of Pulmonary and Allergy Products requested that the Division of Risk Management's Patient Labeling and Education Team review the Applicant's proposed Patient Package Insert (PPI) and Instructions for Use (IFU). This review is written in response to that request.

2 MATERIAL REVIEWED

- TRADENAME Patient Package Insert (PPI) submitted August 1, 2008
- TRADENAME Patient Instructions for Use (IFU) submitted August 1, 2008
- TRADENAME Prescribing Information (PI) submitted August 1, 2008 and revised by the Review Division throughout the current review cycle

3 DISCUSSION

The purpose of patient directed labeling is to facilitate and enhance appropriate use and provide important risk information about medications. Our recommended changes are consistent with current research to improve risk communication to a broad audience, including those with lower literacy.

The draft PPI submitted by the Applicant has a Flesch Kinkaid grade level of 9.1, and a Flesch Reading Ease score of 53.5%. The draft IFU submitted by the Applicant has a Flesch Kinkaid grade level of 4.7, and a Flesch Reading Ease score of 80.4%. To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60% (60% corresponds to an 8th grade reading level).

In our review of the PPI and IFU, we have:

- simplified wording and clarified concepts where possible,
- ensured that the PPI is consistent with the PI,
- removed unnecessary or redundant information
- ensured that the PPI and IFU meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006).

In 2008, The American Society of Consultant Pharmacists Foundation in collaboration with The American Foundation for the Blind published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. They recommend using fonts such as Arial, Verdana, or APHont to make medical information more accessible for patients with low vision. We have reformatted the PPI document

using the font APHont, which was developed by the American Printing House for the Blind specifically for low vision readers.

See the attached document for our recommended revisions to the PPI and IFU. Comments to the review division are ***bolded, underlined and italicized***.

We are providing the review division a marked-up and clean copy of the revised PPI and IFU. We recommend using the clean copy as the working document.

All future relevant changes to the PI should also be reflected in the PPI and IFU.

4 CONCLUSIONS AND RECOMMENDATIONS

TRADENAME (azelastine hydrochloride) Patient Package Insert (PPI)

1. The Applicant's propsed PPI has the following readability scores:
    - Flesch Reading Ease: 53.5%
    - Flesch-Kincaid Grade Level: 9.1

    The sponsor's readability scores for the PPI are higher than that recommended for optimal patient comprehension. We recommend that the Applicant simplify the PPI by incorporating our recommendations.

    Our revised PPI has the following readability scores:
    - Flesch Reading Ease: 58.7%
    - Flesch-Kincaid Grade Level: 7.7

2. Unless "Nasal Spray" is part of the TRADENAME it should not be included as part of the TRADENAME. "Nasal Spray" has been removed throughout this PPI.
3. In the "What is TRADENAME Nasal Spray?" section we removed (b) (4) because this is not a listed indication in the PI. For consistency if the Applicant wishes to add this to the PPI it must first be added to the PI.
4. In the "What should I tell my healthcare provider before using TRADENAME?" section if the risk of hypersensitivity is theoretical with TRADENAME, hypersensitivity should not be listed as a contraindication to use.
5. In the "How should I use TRADENAME Nasal Spray?" section the Applicant should add to section 17 "patient counseling information" instructions on what should be done if the spray gets into the eyes.
6. In the "How should I take TRADENAME?' section the Applicant should clarify if the number of sprays listed include priming sprays.
7. In the "How should I use TRADENAME?" section "if a child accidently swallows TRADENAME Nasal Spray, get medical help or call poison control center right away" this information is important and should be conveyed to patients, but can not be included in patient information unless it is also included in the PI. For consistency if the Applicant wishes to add this to the PPI it must first be added to the PI.
8. In the "What are the possible side effects of TRADENAME Nasal Spray?" section the word (b) (4) was removed because it is not listed as a side effect in the PI. For consistency if the Applicant wishes to add this to the PPI it must first be added to the PI.
9. In the "What are the possible side effects of TRADENAME?" section although not listed in the highlights or in table 1 of section 6.1, "headache" was included in the

PPI because it is listed as a most frequently reported AR (>5%) in section 6.1. The Review Division should clarify if "headache" is a common side effect.

10. In the "How should I store TRADENAME Nasal Spray?" section "do not use TRADENAME Nasal Spray after expiration date "EXP" on the medicine label and box" was removed. We agree that this is an important message however; it is not listed in the PI. If the Applicant wishes to add this to the PPI it must first be added to the PI.

TRADENAME (azelastine hydrochloride) Instructions for Use (IFU)

1. The Applicant's proposed IFU has the following scores:
    - Flesch Reading Ease: 80.4%
    - Flesch-Kincaid Grade Level: 4.7

    The sponsor's readability scores for the IFU are acceptable.

2. In the "For the correct dose of medicine" section the Applicant should add instructions "do not tip your head back". This helps to prevent the medicine from going down the throat. For consistency this information should be added to the Patient Counseling section 17 of the PI.
3. In the "Before you use TRADENAME for the first time, you will need to prime the bottle" section the Applicant should insert a label indicating what is "upright".
4. Figure 5 should be separated into two figures. One should be labeled number 5 and one should be labeled number 6.

Please let us know if you have any questions.

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/s/

LaShawn Griffiths
4/29/2009 04:13:18 PM
DRUG SAFETY OFFICE REVIEWER

Jodi Duckhorn
4/29/2009 08:42:53 PM
DRUG SAFETY OFFICE REVIEWER

SEALD LABELING REVIEW

APPLICATION NUMBER	NDA 22-371
APPLICANT	MEDA Pharmaceuticals
DRUG NAME	ASTEPRO (azelastine hydrochloride) Nasal Spray
SUBMISSION DATE	August 1, 2008
SEALD REVIEW DATE	April 23, 2009
SEALD REVIEWER(S)	Jeanne M. Delasko, RN, MS

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/s/

Jeanne Delasko
4/24/2009 02:25:47 PM
CSO
SEALD comments sent to review division (DPAP) 4/23/2009.

Laurie Burke
4/24/2009 04:24:35 PM
INTERDISCIPLINARY

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications

Memorandum

Date: February 13, 2009

To: Colette Jackson, Regulatory Health Program Manager

From: Jessica Adams, Regulatory Review Officer, DDMAC
Shefali Doshi, Consumer Safety Officer, DDMAC

Subject: NDA 22-371
DDMAC labeling comments for Azelastine Hydrochloride 0.15% Nasal Spray

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DDMAC has reviewed the proposed carton and container labeling, proposed product labeling (PI), and patient product information (PPI) for Azelastine Hydrochloride 0.15% Nasal Spray to the Division of Pulmonary and Allergy Product's consult request submitted on September 3, 2008.

The following comments are provided using the updated version of the proposed PI and PPI, dated December 22, 2008. We offer the following comments on the proposed carton labeling, PI, and PPI.

If you have any questions on the comments for the Prescribing Information, please contact Jessica Adams at (301) 796-3351 or jessica.adams@fda.hhs.gov.

If you have any questions on the comments for the PPI, please contact Shefali Doshi at (301) 796-1780 or **shefali.doshi@fda.hhs.gov.**

Container

- We note that the proposed container labeling includes the trade name (b) (4) Please confirm that the *approved* trade name is used.

Carton

- We note that the proposed carton labeling includes the trade name (b) (4) Please confirm that the *approved* trade name is used.

- The proposed carton labeling makes a representation about the use of the drug by including the term "antihistamine." Therefore, DDMAC recommends either deleting this claim or including the full indication in addition to the most serious and most common risk information for the drug.

- We recommend including information about priming. PI section 2.2 states: "Prime TRADENAME Nasal Spray before initial use by releasing 6 sprays or until a fine mist appears. When TRADENAME Nasal Spray has not been used for 3 or more days, reprime with 2 sprays or until a fine mist appears.").

- The dosing instructions found on the carton labeling inadequately describe the proper procedure for correctly administering the product. We recommend removing these dosing instructions and replacing them with a directive to "Please carefully read the dosing instructions contained inside, before using TRADENAME."

PI

HIGHLIGHTS OF PRESCRIBING INFORMATION

WARNINGS AND PRECAUTIONS

- Should additional context regarding somnolence from section 5.1 be added to the first bullet in this section (i.e., "In clinical trials, the occurrence of somnolence has been reported in some patients taking….")?

- Should additional context from section 5.1 be added to the second bullet in this section (i.e., "additional reductions in alertness and additional impairment of central nervous system performance may occur")?

- The PPI describes the possible side effect of unusual taste as "bitter or (b) (4)" (emphasis added). However, (b) (4) is not noted in the Highlights section. We recommend that the PI and PPI be consistent in terms of the most common adverse reactions.

6 Adverse Reactions

- The PPI describes the possible side effect of unusual taste as "bitter or [(b) (4)] (emphasis added). However, [(b) (4)] is not noted in the Adverse Reactions section. We recommend that the PI and PPI be consistent terms of the most common adverse reactions.

12.3 Pharmacokinetics

- [(b) (4)] Patients
  This section broadens the indication and implies efficacy and safety of azelastine in allergic rhinitis patients [(b) (4)] (emphasis added). Therefore, we recommend deletion.

17 Patient Counseling Information

- Please consider revising the order of this section to disclose the more serious risk information first (i.e., Warnings and Precautions before Common Adverse Reactions)?

- 17.1 Common Adverse Reactions: The PPI describes a possible side effect of unusual taste as "bitter or [(b) (4)] (emphasis added). However, [(b) (4)] is not noted in this section. We recommend that the PI and PPI be consistent terms of the most common adverse reactions.

PPI

(Note that the comment in this section is similar to the comment provided by DDMAC on October 6, 2008, regarding Astepro™ (azelastine hydrochloride) Nasal Spray (NDA 22-203).

1. **What are the possible side effects of TRADENAME Nasal Spray?**

   - "Side effects of TRADENAME Nasal Spray include:
     - unusual taste (bitter [(b) (4)]
     - nose discomfort
     - nosebleeds
     - sneezing

   DDMAC Comment

   The Highlights section of the PI lists bitter taste, nasal discomfort, epistaxis, and sneezing as the most common adverse reactions. However, unusual [(b) (4)] is not listed in the Highlights section or the

Adverse Reactions section of the PI. We recommend that the PPI and PI be consistent in terms of the most common adverse reactions.

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/s/

Jessica Adams
2/17/2009 11:28:49 AM
DDMAC PROFESSIONAL REVIEWER