DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE

Kimberly Skopitz, RAC
Manager, Regulatory Affairs
Meda Pharmaceuticals Inc.
200 North Cobb Parkway, Bldg. 400, Ste. 428
Marietta, GA 30062

RE: NDA 022203
ASTEPRO® (azelastine hydrochloride) Nasal Spray 0.15%
MA #171

Dear Ms. Skopitz:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a professional telephone script (AES11012B) (script) for ASTEPRO® (azelastine hydrochloride) Nasal Spray 0.1% and 0.15% (Astepro 0.15%) submitted by Meda Pharmaceuticals Inc. (Meda) under cover of Form FDA 2253. The script is false or misleading because it presents efficacy claims for Astepro 0.15%, but fails to include any risks associated with its use. In addition, the script overstates the efficacy of Astepro 0.15% and fails to make adequate provision for dissemination of the FDA-approved labeling. Thus, the script misbrands Astepro 0.15% in violation of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), 21 U.S.C. 352(n) & 321(n) and FDA implementing regulations. 21 CFR 202.1(e)(1), (e)(5) & (e)(6)(i).

Background

Below is the indication and summary of the most serious and most common risks associated with the use of Astepro 0.15%.[1]

The INDICATIONS AND USAGE section of the FDA-approved product labeling (PI) states that Astepro 0.15% is "indicated for the relief of the symptoms of seasonal and perennial allergic rhinitis in patients 12 years of age and older."

The PI for Astepro 0.15% contains Warnings and Precautions regarding the risk of somnolence and indicates that patients receiving Astepro should avoid engaging in hazardous occupations requiring complete mental alertness and motor coordination. The PI also indicates that patients should avoid use of alcohol or other central nervous system depressants while using Astepro because additional reductions in alertness and impairment of central nervous system performance may occur. In addition, according to the ADVERSE

[1] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece cited in this letter.

REACTIONS section of the PI, the most commonly reported adverse reactions associated with the use of Astepro 0.15% include bitter taste, nasal discomfort, epistaxis, headache, fatigue, somnolence, and sneezing.

Omission of Risk Information

Promotional materials are misleading if they fail to reveal facts that are material in light of representations made or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials.

The script includes claims regarding efficacy such as, "ASTEPRO® (azelastine hydrochloride) Nasal Spray 0.15% is the first and only nasal antihistamine that is FDA approved for seasonal and perennial allergic rhinitis in patients 12 years of age and older." However, the script entirely omits all risk information associated with the use of Astepro 0.15%. We acknowledge that the script indicates that the purpose of the call is "to share the benefits and important safety information of Astepro 0.15% Nasal Spray" and includes instructions indicating that if an adverse event "is mentioned" the sales representative should "follow the appropriate procedures." However, this is not sufficient to mitigate this misleading presentation. Omission of this information misleadingly suggests that Astepro 0.15% is safer than has been demonstrated.

Overstatement of Efficacy

Promotional materials are misleading if they suggest that a drug is more effective than has been demonstrated by substantial evidence or substantial clinical experience. The script includes the claim, "Also ASTEPRO 0.15% **rapidly** relieves allergic rhinitis symptoms, **including nasal congestion**, without an added decongestant **within 30 to 45 minutes**!" (emphasis added). This claim is misleading because it implies that Astepro is effective in the treatment of the specific symptom of nasal congestion, when this has not been demonstrated by substantial evidence or substantial clinical experience. No references are cited to support this claim. According to the CLINICAL STUDIES section of the PI, the assessment of efficacy for the treatment of seasonal and perennial allergic rhinitis was based on the 12-hour reflective **total** nasal symptom score (rTNSS) in addition to the instantaneous **total** nasal symptom score (iTNSS), where TNSS was calculated as the sum of the patients' scoring of the four individual symptoms of rhinorrhea, nasal congestion, sneezing, and nasal itching. The clinical studies used for approval of Astepro 0.15% evaluated a composite measure of symptoms and did not specifically evaluate efficacy for the individual symptom of nasal congestion. Demonstrating an effect on the composite total nasal symptom score does not represent a clear effect on any individual component of the TNSS. Therefore, the clinical studies used for approval of Astepro 0.15% are not considered substantial evidence to support a claim of efficacy for nasal congestion.

In addition, the above claim misleadingly overstates the efficacy of Astepro 0.15% because it implies that the clinical symptoms of allergic rhinitis will be relieved "rapidly" and "within 30 to 45 minutes" of administration of the drug. OPDP is not aware of substantial evidence or substantial clinical experience to support this claim. If you have data to support this claim, please submit them to FDA for review.

Failure to Fulfill "Adequate Provision" Requirement

The prescription drug advertising regulations require sponsors of broadcast ads to present a brief summary of information relating to side effects and contraindications or, alternatively, make "adequate provision. . . for dissemination of the approved or permitted package labeling in connection with the broadcast presentation." 21 CFR 202.1(e)(1). The script fails to either present a brief summary of required information or make adequate provision for dissemination of the PI.

Conclusion and Requested Action

For the reasons discussed above, the script misbrands Astepro 0.15% in violation of the FD&C Act, 21 U.S.C. 352(n) & 321(n) and FDA implementing regulations. 21 CFR 202.1(e)(1), (e)(5) & (e)(6)(i).

OPDP requests that Meda immediately cease the dissemination of violative promotional materials for Astepro 0.15% such as those described above. Please submit a written response to this letter on or before May 10, 2012, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Astepro 0.15% that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, Division of Professional Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266** or by facsimile at (301) 847-8444. Please note that the Division of Drug Marketing, Advertising, and Communications (DDMAC) has been reorganized and elevated to the Office of Prescription Drug Promotion (OPDP). OPDP consists of the Immediate Office, the Division of Professional Promotion (DPP) and the Division of Direct-to-Consumer Promotion (DDTCP). To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. In addition, OPDP recently migrated to a different tracking system. Therefore, OPDP letters will now refer to MA numbers instead of MACMIS numbers. Please refer to MA # 171 in addition to the NDA number in all future correspondence relating to this particular matter. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Astepro 0.15% comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Roberta Szydlo, R.Ph.
Regulatory Review Officer
Division of Professional Promotion
Office of Prescription Drug Promotion

Lisa Hubbard, R.Ph.
Group Leader
Division of Professional Promotion
Office of Prescription Drug Promotion

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/s/

ROBERTA T SZYDLO
04/26/2012

LISA M HUBBARD
04/26/2012