



Ian C. Reed
Chairman and Chief Executive Officer
Pfizer Inc.
235 East 42nd Street
New York, NY 10017

RE: NDA # 019430
EpiPen[®] and EpiPen[®] Jr. (epinephrine) Auto-Injectors
MA # 388

WARNING LETTER

Dear Mr. Reed:

The Office of Prescription Drug Promotion (OPDP), Division of Consumer Drug Promotion (DCDP) of the U.S. Food and Drug Administration (FDA) has reviewed a 60-second Direct-to-Consumer broadcast television advertisement (TV ad) distributed by Mylan Specialty, L.P. (Mylan) on behalf of Pfizer, Inc. (Pfizer)¹ entitled “Max’s Birthday Party” (EPI12-1003) for EpiPen[®] and EpiPen[®] Jr. (epinephrine) Auto-Injectors (EpiPen). The TV ad was submitted as a complaint to the OPDP Bad Ad Program. The TV ad is false and misleading because it overstates the efficacy of the drug product. Thus, the TV ad misbrands the drug in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 352(n), and FDA implementing regulations. 21 CFR 202.1(e)(6)(i). This violation is particularly alarming from a public health perspective because the misleading presentation of the use of EpiPen may result in serious consequences, including death.

Background²

Below is the indication and summary of the most serious and most common risks associated with the use of EpiPen. According to the FDA-approved EpiPen product labeling (PI) (in pertinent part):

EpiPen[®] and EpiPen[®] Jr Auto-Injectors are indicated in the emergency treatment of allergic reactions (Type I) including anaphylaxis to stinging insects...and biting insects...allergen immunotherapy, foods, drugs, diagnostic testing

¹ Mylan Specialty, L.P. (f/k/a Dey Pharma, L.C.) holds the exclusive license from Meridian Medical Technologies, Inc, a subsidiary of Pfizer, to market, sell, and distribute EpiPen in the United States.

² 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.

substances...and other allergens, as well as idiopathic anaphylaxis or exercise-induced anaphylaxis. EpiPen[®] and EpiPen[®] Jr Auto-Injectors are intended for immediate administration in patients, who are determined to be at increased risk for anaphylaxis, including individuals with a history of anaphylactic reactions.

...

EpiPen[®] and EpiPen[®] Jr Auto-Injectors are intended for immediate self-administration as emergency supportive therapy only and are not a substitute for immediate medical care.

EpiPen is associated with a number of serious risks. According to the PI, EpiPen has Warnings pertaining to the administration, accidental injection, sulfite allergy, and cardiovascular disease, and proper use and storage conditions. In addition, there are Precautions regarding the need for immediate medical care after using EpiPen; caution in patients who have cardiac arrhythmia, coronary artery or organic heart disease; greater risk of developing adverse reactions after epinephrine administration in patients who have hyperthyroidism, cardiovascular disease, hypertension, or diabetes, in elderly, pregnant women, or pediatric patients who require epinephrine doses greater than 0.01 mg/kg; caution with concomitant administration of cardiac glycosides, diuretics, anti-arrhythmics, alpha- and beta-adrenergic blocking agents, tricyclic antidepressants, monoamine oxidase inhibitors, levothyroxine sodium, and certain antihistamines.

Adverse reactions observed with EpiPen are anxiety, apprehensiveness, restlessness, tremor, weakness, dizziness, sweating, palpitations, pallor, nausea and vomiting, headache, respiratory difficulties, arrhythmias, hypertension, and angina.

Overstatement of Efficacy

Promotional materials are misleading if they contain representations or suggestions that a drug is better or more effective than has been demonstrated by substantial evidence or substantial clinical experience. The TV ad includes the following presentation (bolded emphasis original):

- Mother: “Excited for Max’s birthday party? Should be pretty awesome.”
- Son: “Yeah!”
- Mother: “Even with your peanut allergy and a cake made of who-knows-what.”

SUPER (over visual): EpiPen[®] (epinephrine) Auto-Injector can’t eliminate the risk of anaphylaxis. [frames 1 to 2]

- Mother: “Because we’re prepared, right Jake?”
- Son: “Yup!”
- Mother: “With EpiPen.”

SUPER (over visual): Be prepared. With EpiPen[®]. EpiPen[®] (epinephrine) Auto-Injector can't eliminate the risk of anaphylaxis. [frame 3]

The overwhelming impression conveyed by this presentation in the TV ad is that EpiPen *alone* can provide assurance that a child who has a history of life-threatening allergic reactions does not need to worry or take precautionary measures to avoid exposure to allergens. Specifically, the TV ad misleadingly suggests that a child who has a peanut allergy can take a chance eating a piece of birthday cake with unknown ingredients and feel completely free from worry about any potential risk of anaphylaxis if prepared with EpiPen. This claim is misleading because it implies that EpiPen *alone* obviates the need for taking precautionary measures and provides protection against any potential risks due to exposure to an allergen, when this has not been demonstrated by substantial evidence or substantial clinical experience. According to the INDICATIONS and USAGE section of the PI (emphasis added), "EpiPen[®] and EpiPen[®] Jr Auto-Injectors are intended for immediate self-administration as emergency supportive therapy . . ." In addition, the **What is the most important information I should know about EpiPen[®] and EpiPen[®] Jr Auto-Injector** section of the FDA-approved Patient Labeling states (bolded emphasis original, underlined emphasis added), "**When you have an allergic reaction (anaphylaxis) use the EpiPen[®] or EpiPen[®] Jr Auto-Injector right away and immediately go to your doctor or emergency room for more medical treatment.**" We note the SUPER, "EpiPen[®] (epinephrine) Auto-Injector can't eliminate the risk of anaphylaxis." However, this does not mitigate the overall misleading impression. The standard of care to prevent a potentially life-threatening anaphylactic reaction is to take precautionary measures to avoid the allergen.

Conclusion and Requested Action

For the reasons described above, the TV ad misbrands EpiPen in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 352(n), and FDA implementing regulations. 21 CFR 202.1(e)(6)(i).

OPDP acknowledges that, following a teleconference with OPDP and Pfizer on April 20, 2012, during which OPDP outlined its serious concerns with the piece discussed above, Pfizer committed to comply with OPDP's request to immediately cease the dissemination of this material and any materials with the same or similar claims for EpiPen. We appreciate this commitment and the steps that Pfizer has taken thus far to address some of the issues outlined in this letter.

OPDP requests that Pfizer submit a written response to this letter on or before June 7, 2012, listing all promotional materials (with the 2253 submission date) for EpiPen that contain the same or similar claims for EpiPen described above and discussed during the April 20, 2012, teleconference, and explaining your plan for discontinuing use of such violative materials. Because the violation described above is serious, we request, further, that your submission include a comprehensive plan of action to disseminate truthful, non-misleading, and complete corrective messages about the issues discussed in this letter to the audience(s) that received the violative promotional materials. In order to clearly identify the violative promotional

piece(s) and/or activity and focus on the corrective message(s), OPDP recommends that corrective piece(s) include a description of the violative promotional piece(s) and/or activity, include a summary of the violative message(s), provide information to correct each of the violative message(s), and be free of promotional claims and presentations. To the extent possible, corrective messaging should be distributed using the same media, and generally for the same duration of time and with the same frequency that the violative promotional material was disseminated.

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 Direct-to-Consumer Promotion, 5901-B Amundson Avenue, 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 Drug Promotion (DPDP) and the Division of Consumer Drug Promotion (DCDP). 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 # 388 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 EpiPen comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Failure to correct the violations discussed above may result in FDA regulatory action, including seizure or injunction, without further notice.

Sincerely,

{See appended electronic signature page}

Robert Dean, MBA
Division Director
Division of Consumer Drug Promotion
Office of Prescription Drug Promotion

Ian C. Reed
Pfizer Inc.
NDA # 019430 / MA # 388

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cc: John Thievon
President
Mylan Specialty L.P.
110 Allen Road, 4th Floor
Basking Ridge, NJ 07920

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ROBERT T DEAN
05/24/2012