DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Henry A. McKinnell, Jr., Ph.D.
Chairman of the Board
and Chief Executive Officer
Pfizer Inc.
235 East 42nd Street
New York, NY 10017

Re: NDA 19-835, 20-346, 21-621
Zyrtec® (cetirizine HCl) Tablets, Syrup, and Chewable Tablets
MACMIS # 12799

WARNING LETTER

Dear Dr. McKinnell:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed three direct-to-consumer (DTC) print advertisements (ads) titled "Tired of your allergy medicine not working?" (airplane) (ID #ZY179738), "Tired of your allergy medicine not working?" (office) (ID #ZY182060A) and "Maybe it's time to switch allergy medicines" (ID #ZY182060) for Zyrtec® (cetirizine HCl) Tablets, Syrup, and Chewable Tablets submitted by Pfizer Inc. (Pfizer) under cover of Form FDA 2253. The print ads make superiority claims about Zyrtec by suggesting it is clinically superior to some other allergy medicines. To our knowledge, these claims have not been demonstrated by substantial evidence or substantial clinical experience. Therefore, these claims misbrand your drug product in violation of the Federal Food, Drug, and Cosmetic Act (Act) and FDA implementing regulations. See 21 U.S.C. § 352(n); 21 CFR 202.1(e)(6).

Background

Approved Product Labeling

According to the approved product labeling (PI), Zyrtec is FDA-approved for the following indications:

> **Seasonal Allergic Rhinitis [SAR]**: ZYRTEC is indicated for the relief of symptoms associated with seasonal allergic rhinitis due to allergens such as ragweed, grass and tree pollens in adults and children 2 years of age and older. Symptoms treated effectively include sneezing, rhinorrhea, nasal pruritus, ocular pruritus, tearing, and redness of the eyes. **Perennial Allergic Rhinitis [PAR]**: ZYRTEC is indicated for the relief of symptoms associated with perennial allergic rhinitis due to allergens such as dust mites, animal dander and mold in adults and children 6 months of age and older. Symptoms treated effectively include sneezing, rhinorrhea, postnasal discharge, nasal pruritus, ocular pruritus, and tearing.

According to the PI, the most common adverse reactions associated with the use of Zyrtec in persons 12 years and older include somnolence, fatigue, and dry mouth.

The Zyrtec PI also includes a specific precaution regarding somnolence, which states that "due caution should…be exercised when driving a car or operating potentially dangerous machinery. Concurrent use of ZYRTEC with alcohol or other CNS depressants should be avoided because additional reductions in alertness and additional impairment of CNS performance may occur."

Regulatory History

DDMAC has sent you three previous untitled letters for Zyrtec Tablets/Syrup since 1998. On March 4, 1998, DDMAC issued an untitled letter on a sales brochure that made implied clinical superiority claims based on comparative pharmacodynamic data, but which were not supported by substantial evidence or substantial clinical experience. On December 21, 1998, DDMAC issued an untitled letter on the dissemination of a bibliography of "Abstracts of Selected Zyrtec Literature," which listed abstracts that promoted the superiority of Zyrtec over other antihistamines in the absence of substantial evidence or substantial clinical experience to support that claim, as well as a detailer that implied an unsubstantiated risk of serious cardiovascular events with Claritin. On April 30, 2002, DDMAC issued an untitled letter on a DTC broadcast ad for failing to disclose risk information and for failing to make adequate provision for dissemination of the PI.

On July 8, 2003, DDMAC and the Federal Trade Commission (FTC) sent a joint letter to Pfizer expressing our concerns about promotional materials that compared Zyrtec to other allergy medicines, and which specifically communicated the concern that "consumers might misinterpret these claims as suggesting that Zyrtec has been demonstrated to work better at treating PAR symptoms than other allergy medicines or that the other medicines have been demonstrated to be ineffective for treating PAR symptoms." The letter further stated:

> "We are unaware of any evidence that Zyrtec is clinically superior to various OTC and prescription oral allergy medicines. Nor are we aware of evidence that other antihistamines are not effective in PAR. It is therefore important that your advertising distinguish between having evidence of effectiveness in, and approval for, PAR, as Zyrtec does, and any suggestion that Zyrtec is actually more effective."

Unsubstantiated Superiority Claims

The three DTC print ads cited above make false or misleading claims that Zyrtec is clinically superior to some other allergy medicines, namely, that Zyrtec "works" and that at least some other allergy medicines do not work.

The "Tired of your allergy medicine not working?" (airplane) ad features a picture of two people seated on an airplane. A man is sneezing and the text next to his picture states: "In the right seat. On the wrong allergy medicine." The woman in the seat next to him, who is not sneezing, is looking at him. The text next to her picture states: "On top of things. On Zyrtec." The prominent callout

headline below the picture states “Tired of your allergy medicine not working? Good thing there’s Zyrtec.”

The “Tired of your allergy medicine not working?” (office) ad features a picture of people in an office setting. A woman appears to be sneezing into a tissue, and the text next to her picture states: “On the wrong page. On the wrong allergy medicine.” The woman next to her is on the phone and is looking over at her, with the text next to her picture stating: “On the ball. On Zyrtec.” The prominent callout headline below the picture states “Tired of your allergy medicine not working? Good thing there’s Zyrtec.”

The “Maybe it’s time to switch allergy medicines” ad features the same office setting as the prior ad. The text next to the woman wiping her nose states: “Needs to switch allergy medicines.” The text next to the woman on the phone states: “Needs to switch desks.” The prominent callout headline below the picture states: “Maybe it’s time to switch allergy medicines when your co-worker volunteers to swap seats with the intern.”

For each of the ads, the text under the headline states: “Your allergy medicine should work on all of your indoor and outdoor allergies. Really work. Why put up with a medicine that only treats outdoor allergies? Shouldn’t it cover both?” Each ad also tells the consumer to ask their doctor “about switching to prescription Zyrtec,” “So you – and your seatmates – can feel good the whole flight” or “So you – and your co-workers – can feel good in the office,” respectively.

The overwhelming message from the text and the visuals of these ads is the comparative claim that Zyrtec is more effective in treating allergies in general, or certain types of allergies, than some other allergy products, which are not effective. As noted above, FDA is not aware of substantial evidence or substantial clinical experience demonstrating that Zyrtec is clinically superior to any other available OTC and prescription oral allergy medicine. In addition, it is misleading to suggest that patients taking Zyrtec would be “On top of things” or “On the ball” as compared to patients on other allergy drugs. Furthermore, FDA is not aware of substantial evidence or substantial clinical experience demonstrating that other antihistamines are not effective in treating PAR (i.e., have been tested and failed), as is suggested by these ads. Finally, FDA is not aware of substantial evidence or substantial clinical experience showing that patients who fail on other allergy drugs will be effectively treated by Zyrtec, as the ad suggests. Therefore, these claims are false or misleading.

FDA does not object to the dissemination of truthful, non-misleading statements about approved indications, and we acknowledge that Zyrtec is approved for a broader range of indications than many other antihistamines. Therefore, we do not object to the statement in the ads that, "No other antihistamine is approved to treat more allergies than Zyrtec." Rather, our concern is that this factual statement, which follows the other claims and visuals noted above, does not correct the overall misleading impression that superior effectiveness, not merely a comparison of indications, is being promoted in these ads. Absent substantial supporting evidence or clinical experience, the ads suggest that the absence of a particular claim in another antihistamine's labeling affirmatively means that the antihistamine does not work for that claim. Likewise, they also suggest that Zyrtec is more effective -- either in general or in specific cases -- than at least some other antihistamines.

Conclusion and Requested Action

The DTC print ads "Tired of your allergy medicine not working?" and "Maybe it's time to switch allergy medicines" make false or misleading claims that Zyrtec is clinically superior to other allergy medicines (21 U.S.C. § 352(n); 21 CFR 202.1(e)(6)).

DDMAC requests that Pfizer immediately cease the dissemination of violative promotional materials for Zyrtec that contain claims the same as or similar to those described above. Please submit a written response to this letter on or before April 27, 2005, stating whether you intend to comply with this request, listing all violative promotional materials for Zyrtec that contain claims the same as or similar to those described above, and explaining your plan for discontinuing use of such materials. Because the violation described above is serious and repeated, 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. Please direct your response to me at the Food and Drug Administration, 5600 Fishers Lane, HFD-42, Room 8B-45, Rockville, MD, 20857, facsimile at (301) 594-6759. In all future correspondence regarding this matter, please refer to MACMIS #12799 in addition to the NDA number. We remind 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 Zyrtec comply with each applicable requirement of the Act and FDA implementing regulations.

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

Sincerely,

{See appended electronic signature page}

Thomas W. Abrams, RPh, MBA
Director
Division of Drug Marketing,
Advertising, and Communications

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

/s/

Thomas Abrams

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