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November 1, 2004
Thomas W. Abrams
Director
Office of Medical Policy Division of Drug Marketing, Advertising, and Communications
Food and Drug Administration

Re: Failure to disclose suicide warnings in Zoloft advertisement

Dear Dr. Abrams:

The purpose of this letter is to file a complaint about a two-page Pfizer advertisement for their antidepressant drug, Zoloft, which appeared in the Sunday New York Times Magazine (October 24, 2004). The ad failed to include ANY of the FDA required warnings about the increased suicide risk for patients taking Zoloft. The ad claims "Zoloft [is] working to correct the chemical imbalance," stating: "Side effects may include dry mouth, insomnia, sexual side effects, diarrhea, nausea and sleepiness."

The FDA Division of Drug Marketing, Advertising and Communications requires that companies that advertise directly to consumers must "include ALL risk information in a product's approved label…In addition to the specific disclosure requirements, advertisements cannot be false or misleading or omit material facts." [See: http://www.fda.gov/cder/ddmac/FAQS.HTM]

In its March 22, 2004 advisory, the FDA informed antidepressant drug manufacturers that they would have to revise their drugs' labels to include extensive warnings about the suicide risk, and what families and caregivers must be on the look out for.
Pfizer's October 24 advertisement in The Times violated fundamental FDA requirements by failing to include "specific disclosure requirements" and by "omit[ting]material facts" about risks—in this case, life-threatening risks. The reproduced Zoloft Brief Summary (of the label) is grossly misleading about the suicide risk when it states:

"The possibility of a suicide attempt is inherent in major depressive disorder and may persist until significant remission occurs. Close supervision of high risk patients should accompany

initial drug therapy."

As you know, on October 15, 2004, the FDA announced heightened warnings for all antidepressants—including Zoloft. These drugs labels are required to include Black Box warnings, acknowledging that a causal relationship has been established between antidepressants and an increased risk of suicide. The wording in the black box warnings must conform to FDA-approved language.

The decision requiring a Black Box warning for antidepressants comes after a protracted, deliberative process which many have criticized as foot dragging. The FDA held two advisory committee meetings, conducted three separate analyses of the pediatric clinical trial data, and issued three public advisories (June 19, 2003; October, 2003; and March 22, 2004).

The following section, formatted as it appears in the revised Zoloft label--with bold in the original—conforms with the FDA March 22, 2004 requirement. The Zoloft label was approved on August 19, 2004. (Almost identical language and formatting appears on the labels of the other SSRI antidepressants).

WARNINGS:

"Clinical Worsening and Suicide Risk

Patients with major depressive disorder, both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality), whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Although there has been a long-standing concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients, a causal role for antidepressants in inducing such behaviors has not been established. **Nevertheless, patients being treated with antidepressants should be observed closely for clinical worsening and suicidality, especially at the beginning of a course of drug therapy, or at the time of dose changes, either increases or decreases.** Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse or whose emergent suicidality is severe, abrupt in onset, or was not part of the patient's presenting symptoms.

Because of the possibility of co-morbidity between major depressive disorder and other psychiatric and nonpsychiatric disorders, the same precautions observed when treating patients with major depressive disorder should be observed when treating patients with other psychiatric and nonpsychiatric disorders.

The following symptoms: anxiety, agitation, panic attacks, insomnia, irritability, hostility (aggressiveness), impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients for whom such symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, **should be alerted about the need to monitor patients for the emergence of agitation, irritability, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers.**

> Prescriptions for ZOLOFT should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose. If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms (see PRECAUTIONS and DOSAGE AND ADMINISTRATION, Discontinuation of Treatment with ZOLOFT, for a description of the risks of discontinuation of ZOLOFT).
> It should be noted that ZOLOFT is approved in the pediatric population only for obsessive compulsive disorder.
>
> A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that ZOLOFT is not approved for use in treating bipolar depression."

Pfizer's October 24 ad failed to disclose the risks that Zoloft poses. It also failed to disclose a "clinically important" risk of weight loss in children taking Zoloft (sertraline). Children who develop normally should be gaining weight and height. The weight loss risk is disclosed in the FDA-approved label (2003, 2004) but not in the advertisement.

> "There was a bigger difference between sertraline and placebo in the proportion of outliers for clinically important weight loss in children than in adolescents. For children, about 7% had a weight loss >7% of body weight, compared to none in the placebo patients; for adolescents, 2% had a weight loss >7% of body weight compared to 1% of placebo patients."

Pfizer's October advertisement in The New York Times magazine is a gross violation of FDA's Division of Drug Marketing, Advertising and Communications regulations. The ad omitted vital material facts about Zoloft related risks eight months after the FDA ordered label revisions for all antidepressants, requiring the suicide risk to be disclosed. The ad was disseminated without warnings even after the FDA ordered heightened, black box warnings for Zoloft. The ad was disseminated to millions of consumers whom the company misled about the safety of its product.

Proposed remedy: Pfizer should not only be ordered to stop all such deceptive advertising immediately, but the company should be required to publish full page corrective statements acknowledging its failure to disclose the risks in its advertisement as is required by the FDA. The correction should reproduce the "Clinical Worsening and Suicide Risk" section and the "Black Box" warning, and should be published in the same publications in which the ad ran so that it reaches the same audience that the false and misleading advertisement did.

The FDA is both authorized and responsible for the dissemination of accurate information and disclosure of risks posed by FDA-approved drugs. Unfortunately, FDA's failure to enforce drug marketing standards has resulted in the dissemination of blatant false drug advertisements.

Sincerely,

Vera Hassner Sharav

THE ALLIANCE FOR HUMAN RESEARCH PROTECTION

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cc: Lester Crawford
Attorney General Eliot Spitzer
Senator Chuck Schumer
Senator Chuck Grassley
Congressman Joe Barton
Congressman Henry Waxman
Congressman Maurice Hinchey

Russell Lewis President and Chief Executive Officer, The New York Times