DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Pfizer Pharmaceuticals
Mojgan M. Moghaddassi, PharmD
Regulatory Affairs
235 East 42nd Street
New York, NY 10017-3184

RE: NDA #19-839
Zoloft® (sertraline HCl) Tablets
MACMIS #13073

Dear Dr. Moghaddassi:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed a direct-to-consumer (DTC) print advertisement (ad) for Zoloft® (sertraline HCl) Tablets from the October 24, 2004, issue of the New York Times magazine. The print ad is false or misleading because it omits important information relating to the risk of suicidality in patients taking Zoloft, in violation of the Federal Food, Drug, and Cosmetic Act (Act) (21 U.S.C. 352(n)) and FDA implementing regulations, 21 CFR 202.1 (e)(5)(iii) and (e)(3)(iii). This ad is concerning from a public health perspective because it fails to include a serious risk associated with the drug.

Background

Zoloft is an orally administered psychotropic drug approved for treatment of major depressive disorder (among other uses) in adults. The Warnings section of the FDA-approved labeling (PI), as of October 24, 2004, stated (in pertinent part):

> **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.

In addition, the Precautions-Information for Patients section of the PI states that patients should be monitored for panic attacks, hostility (aggressiveness), agitation, anxiety, insomnia, and suicidal ideation when being treated with Zoloft, especially early during treatment. Such symptoms should be reported to the patient's physician, especially if they are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

Communications

On March 19, 2004, the Division of Neuropharmacological Drug Products (DNDP) asked Pfizer to include a new subsection under the Warnings section of the PI regarding clinical worsening and suicidality risk. In addition, DNDP requested that the Precautions-Information for Patients section be revised to include symptoms of suicidal ideation. DNDP approved Pfizer's new labeling language on May 21, 2004, and Pfizer incorporated these changes into a new PI in July 2004.

Omission of Material Fact

The print ad is misleading because it fails to reveal material facts "with respect to consequences that may result from use of" Zoloft as described in the PI. See 21 CFR 202.1 (e)(5)(iii). Specifically, the main page of the ad fails to communicate <u>any</u> information pertaining to the risk of clinical worsening and suicidality in patients who are on Zoloft therapy. Furthermore, the brief summary page of the ad is excerpted from an outdated September 2003 PI, rather than the most current version of the PI as of the time the ad was run (July 2004 PI), and therefore omits the subsection from the Warnings section of the July 2004 PI regarding the risk of clinical worsening and suicidality.

Conclusion and Requested Action

For the reasons discussed above, the print ad misbrands Zoloft under section 502(n) of the Act, 21 U.S.C. 352(n), and FDA implementing regulations, 21 CFR 202.1(e)(5)(iii) and (e)(3)(iii).

DDMAC requests that Pfizer immediately cease the dissemination of promotional materials for Zoloft the same as or similar to those described above. Please submit a written response to this letter on or before May 20, 2005, describing your intent to comply with this request, listing all promotional materials for Zoloft the same as or similar to those described above, and explaining your plan for discontinuing use of such materials. Please direct your response to me at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm. 8B-45, 5600 Fishers Lane, Rockville, Maryland 20857, facsimile at (301) 594-6759. In all future correspondence regarding this matter, please refer to NDA #19-839 and MACMIS #13073. 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 Zoloft comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Kay A. Chitale, PharmD
Consumer Promotion Analyst
Regulatory Review Officer
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/

Kay Chitale

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