DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Robert B. Clark
Vice-President, US Regulatory
Pfizer Inc.
235 East 42nd Street
New York, New York, 10017
Fax (212) 672-7807

RE: NDA # 20-919
Geodon (ziprasidone mesylate) for Injection
MACMIS ID # 15144

Dear Mr. Clark:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) of the U.S. Food and Drug Administration (FDA) has reviewed a professional journal advertisement (GZ270749A) for Geodon (ziprasidone mesylate) for Injection submitted by Pfizer Inc. (Pfizer) under cover of Form FDA 2253. This piece is false or misleading because it omits important risk information and contains unsubstantiated superiority claims. Thus, the promotional material misbrands the drug in violation of the Federal Food, Drug, and Cosmetic Act (Act), 21 U.S.C. 352(n) & 321(n). *Cf*. 21 CFR 202.1(e)(5)(i); (5)(iii); (e)(6)(i); (e)(6)(ii).

Background

According to its FDA-approved product labeling (PI), Geodon for Injection is indicated for the treatment of acute agitation in schizophrenic patients for whom treatment with ziprasidone is appropriate and who need intramuscular (IM) antipsychotic medication for rapid control of the agitation.

Geodon for Injection is associated with a number of serious risks, some of which are potentially fatal. The PI for Geodon for Injection includes a black box warning concerning increased mortality in elderly patients with dementia-related psychosis. Furthermore, there are contraindications and warnings concerning the use of Geodon for Injection in patients with a known history of QT prolongation (including congenital long QT syndrome), recent acute myocardial infarction, or with uncompensated heart failure and in patients on concomitant therapy with other medications that can prolong the QT interval. The QT warning states that “Some drugs that prolong the QT/QTc interval have been associated with the occurrence of torsade de pointes and with sudden unexplained death.” The PI also includes warnings for neuroleptic malignant syndrome, tardive dyskinesia, and hyperglycemia and diabetes mellitus, as well as a number of precautions including rash, orthostatic hypotension, and seizures.

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Omission of Important Risk Information

Promotional materials are false or misleading if they fail to reveal facts that are material in light of the representations made or with respect to consequences that may result from the use of the drug as recommended or suggested in the materials. While the journal ad discusses the boxed warning for increased mortality in elderly patients with dementia-related psychosis, the warning for QT prolongation, and a list of the most commonly observed adverse events, it fails to communicate other serious warnings and precautions associated with Geodon for Injection use. Specifically, the journal ad fails to include the warnings for neuroleptic malignant syndrome, tardive dyskinesia, and hyperglycemia and diabetes mellitus. The journal ad does mention "movement disorders" and "low EPS," and while we do not object to these claims, the presentations are insufficient to communicate the risk concepts associated with, and the seriousness of, tardive dyskinesia. Additionally, the professional journal ad fails to include important precautions, specifically, rash, orthostatic hypotension, and seizures. By omitting these risks, the journal ad misleadingly suggests that Geodon for Injection is safer than has been demonstrated.

Unsubstantiated Superiority Claims

Promotional materials are false or misleading if they contain a drug comparison that represents or suggests that a drug is safer or more effective than another drug in some particular when this has not been demonstrated by substantial evidence or substantial clinical experience. The professional journal ad claims:

> " • Proven advantages over haloperidol IM
> —twice the improvement as measured on the BPRS"[1]

This presentation is misleading because it implies that Geodon for Injection is more effective than haloperidol IM when this has not been demonstrated by substantial evidence or substantial clinical experience. The single study cited for this claim was an open-label study, which is not an appropriate study design to evaluate subjective endpoints, such as those measured by the Brief Psychiatric Rating Scale anchored version (BPRS), because of the potential for evaluator bias. In fact, FDA is not aware of any substantial evidence to support this claim. If you have data, please submit them to FDA for review. Of interest, in the clinical trials submitted to the NDA for Geodon for Injection, the BPRS was not used and there were no active comparators.

Conclusion and Requested Action

For the reasons discussed above, the professional journal ad misbrands Geodon for Injection in violation of the Federal Food, Drug, and Cosmetic Act (Act), 21 U.S.C. 352(n) & 321(n). *Cf.* 21 CFR 202.1(e)(5)(i); (5)(iii); (e)(6)(i); (e)(6)(ii).

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[1] Brook S, Lucey JV, Gunn KP, for the Ziprasidone IM Study Group. Intramuscular ziprasidone compared with intramuscular haloperidol in the treatment of acute psychosis. *J Clin Psychiatry*. 2000;61:933-941

DDMAC requests that Pfizer immediately cease the dissemination of violative promotional materials for Geodon for Injection such as those described above. Please submit a written response to this letter on or before July 27, 2007, stating whether you intend to comply with this request, listing all violative promotional materials for Geodon for Injection 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, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD 20705-1266, or facsimile at 301-796-9878. In all future correspondence regarding this matter, please refer to MACMIS # 15144 in addition to the NDA number. We remind you that only written communications are considered official. If you choose to revise your promotional materials, DDMAC is willing to assist you with your revised materials by commenting on your revisions before you use them in promotion.

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

Sincerely,

{See appended electronic signature page}

Robert Dean, MBA
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/

Jialynn Wang
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Signed for Robert Dean, MBA