



NDA 18-276/S-038, 039

NDA 21-434/S-001

Pfizer, Inc.
c/o Pharmacia and Upjohn Company
Attention: Alan Dunbar, Director
235 East 42nd Street
150/7/16
New York, NY 10017

Dear Mr. Dunbar:

Please refer to your supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Application	Drug Name	Submission Date	Receipt Date	Provides For:
NDA 21-434/ SLR-001	Xanax XR (alprazolam) Extended-Release Tablets	March 11, 2003	March 12, 2003	Update to PRECAUTIONS/Drug Interactions section of labeling to include additional guidance to the physician regarding potential drug interactions of alprazolam with sertraline and paroxetine.
NDA 18-276/ SLR-038	Xanax (alprazolam) Tablets	April 2, 2003	April 3, 2003	
NDA 18-276/ SLR-039	Xanax (alprazolam) Tablets	October 1, 2003	October 2, 2003	Revisions to various sections of the current Xanax labeling to be consistent with the recently approved Xanax XR labeling.

We have completed our review of these applications and they are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

We remind you of your email communication on April 1, 2004 in which you committed to the following labeling language under the section entitled, "Drug Interactions":

Drugs and other substances demonstrated to be CYP3A inhibitors on the basis of clinical studies involving benzodiazepines metabolized similarly to alprazolam or on the basis of in vitro studies with alprazolam or other benzodiazepines (caution is recommended during coadministration with alprazolam).

Available data from clinical studies of benzodiazepines other than alprazolam suggest a possible drug interaction with alprazolam for the following: diltiazem, isoniazid, macrolide antibiotics such as erythromycin and clarithromycin, and grapefruit juice. Data from in vitro studies of alprazolam suggest a possible drug interaction with alprazolam for the following: sertraline and paroxetine. However, data from an in vivo drug interaction study involving a single dose of alprazolam 1 mg and steady state doses of sertraline (50 to 150 mg/day) did not reveal any clinically significant changes in the pharmacokinetics of alprazolam. Data from in vitro studies of benzodiazepines other than alprazolam suggest a possible drug interaction for the following: ergotamine, cyclosporine, amiodarone, nicardipine, and nifedipine. Caution is recommended during the coadministration of any of these with alprazolam (see WARNINGS).

The final printed labeling (FPL) must be identical to the labeling text submitted for the package inserts including the agreed upon labeling listed above.

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 18-276/S-038, 039 and NDA 21-434/S-001." Approval of these submissions by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Richardae Taylor, Pharm.D., Regulatory Health Project Manager, at (301) 594-5793.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

Thomas Laughren
4/2/04 10:30:14 AM
Signed for Russell Katz, M.D.