



NDA 19-949/S-048
NDA 19-950/S-053
NDA 20-090/S-031

SUPPLEMENTS APPROVAL

Pfizer, Inc.
Attention: Ms. Beatrice Curran
Associate Director
Worldwide Regulatory Strategy
235 East 42nd Street 685/19/05
New York, NY 10017-5755

Dear Ms. Curran:

Please refer to your supplemental new drug applications (sNDAs) dated February 5, 2010, received February 5, 2010, and submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product	NDA Number	Supplement Number
Diflucan (fluconazole) Tablets, 50 mg, 100 mg, and 200 mg	19-949	S-048
Diflucan (fluconazole) I.V., 2 mg/mL	19-950	S-053
Diflucan (fluconazole) for Oral Suspension, 10 mg/mL and 40 mg/mL	20-090	S-031

SUMMARY OF LABELING SUPPLEMENTS

These “Changes Being Effected” supplemental new drug applications provide for the addition of information regarding food effect to the package insert, and were submitted in response to our supplement request letter dated December 22, 2009 to NDAs 19-949 and 19-950.

We requested that you update labeling for Diflucan after we reviewed your May 12, 1992 submission to IND 27,283, reporting on Post-Marketing Commitment (PMC) #1: “Study the effect of food on the bioavailability of a tablet dosage form to be marketed.” This PMC was included in the original January 29, 1990 approval letter for NDAs 19-949 and 19-950.

NDA 20-090 was approved subsequently on December 23, 1993; it did not include PMC #1. Given that NDAs 19-949, 19-950 and 20-090 share the same package insert, the revisions regarding food effect apply to all three NDAs.

REVISIONS TO THE PACKAGE INSERT

The following revisions to the package insert (PI) that were agreed upon for the above supplements (additions are noted with underline and deletions with ~~strikethrough~~):

- a. Under the **CLINICAL PHARMACOLOGY/Pharmacokinetics and Metabolism** subsection, a new fourth paragraph was added after paragraph three, as shown below:

In fasted normal volunteers, administration of a single oral 400 mg dose of DIFLUCAN (fluconazole) leads to a mean C_{max} of 6.72 µg/mL (range: 4.12 to 8.08 µg/mL) and after single oral doses of 50-400 mg, fluconazole plasma concentrations and AUC (area under the plasma concentration-time curve) are dose proportional.

The C_{max} and AUC data from a food-effect study involving administration of DIFLUCAN (fluconazole) tablets to healthy volunteers under fasting conditions and with a high-fat meal indicated that exposure to the drug is not affected by food. Therefore, DIFLUCAN may be taken without regard to meals. (see **DOSAGE AND ADMINISTRATION.**)

- b. Under the **DOSAGE AND ADMINISTRATION/Administration** subsection, the first paragraph was revised as follows:

DIFLUCAN may be administered either orally or by intravenous infusion. DIFLUCAN can be taken with or without food. DIFLUCAN injection has been used safely for up to fourteen days of intravenous therapy. The intravenous infusion of DIFLUCAN should be administered at a maximum rate of approximately 200 mg/hour, given as a continuous infusion.

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text, including minor editorial revisions.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling (text for the package insert) and include the labeling changes proposed in any pending “Changes Being Effectuated” (CBE) supplements. Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories. Also within 14 days, amend all pending supplemental applications for these NDAs, including pending “Changes Being Effected” (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format that includes the changes approved in this supplemental application.

LABELING

Submit final printed labeling as soon as it is available, but no more than 30 days after it is printed. The final printed labeling (FPL) must be identical to the package insert. The final printed labeling should be submitted electronically according to the guidance for industry titled “Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)”. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate these submissions “**Final Printed Labeling for approved NDA 19-949/S-048; NDA 19-950/S-053; NDA 20-090/S-031**” Approval of these submissions by FDA is not required before the labeling is used.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about these drug products (i.e., a “Dear Health Care Professional” letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

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

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If you have any questions, call Jacquelyn Smith, M.A., Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and Transplant Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure: Package Insert (PI)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20090	SUPPL-31	PFIZER CHEMICALS DIV PFIZER INC	DIFLUCAN
NDA-19950	SUPPL-53	PFIZER INC	DIFLUCAN IN DEXTROSE 5% IN PLASTIC CONTA
NDA-19949	SUPPL-48	PFIZER CENTRAL RESEARCH	DIFLUCAN

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

/s/

RENATA ALBRECHT
08/05/2010