



NDA 50-718/S-010

Alza Corporation
Attention: Jannel Wissel
Sr. Vice President, Operations
1900 Charleston Road
P.O. Box 7210
Mountain View, CA 94039-7210

Dear Ms. Wissel:

Please refer to your supplemental new drug application dated September 27, 2001, received October 2, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Doxil® (doxorubicin HCl liposome injection).

This "Changes Being Effected" supplemental new drug application provides for proposed changes to conform to recommendations made in our January 31, 2001 approval letter. In addition, item 2 in the Boxed Warnings and Infusion Reactions subsection, under the WARNINGS section, have been strengthened based on a review of post-marketing reports.

We have reviewed the labeling that you submitted in accordance with our January 31, 2001 letter, and the supplemental application is approved effective on the date of this letter.

However, the following should be corrected at the next printing or within 6 months, whichever comes first. This revision may be submitted as "Change Being Effected."

1. Under the Myelosuppression subsection of the WARNINGS section, the second sentence of the paragraph "[ANC < 1000]" should be added after the word neutropenia as follows:

"Anemia was the most ... (24.2%) and neutropenia [ANC < 1000] (19.0%) ..."

2. Under the Infusion Reactions subsection of the WARNINGS section, please add back the following sentence to the first paragraph.

"Six AIDS-KS patients (0.9%) and 13 (1.7%) solid tumor patients discontinued Doxil® therapy because of infusion related reactions."

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted September 27, 2001).

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavyweight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 50-718/S-010." Approval of this submission by FDA is not required before the labeling is used.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call Patty Garvey, Regulatory Project Manager, at 301-594-5766.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Director
Division of Oncology 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
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/s/

Richard Pazdur
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