DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-212/S-004/S-005/S-006

Pharmacia & Upjohn Company
Unit 0635-298-113
7000 Portage Road
Kalamazoo, MI 49001-0199

Attention: Carl M. DeJuliis, MS, RPh
Regulatory Manager, Regulatory Affairs

Dear Mr. DeJuliis:

Please refer to your supplemental new drug applications dated August 17, 1999 (S-004), November 28, 2000 (S-005), and December 28, 2001 (S-006) received August 19, 1999, November 30, 2000, and December 31, 2001 respectively, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ZINECARD™ for Injection (dexrazoxane for injection).

We acknowledge receipt of your submissions dated September 5, 2002 (S-005), February 21, 2002 (S-006) and October 29, 2002 (2) (S-005 and S-006).

Supplement 004 provides for the addition of a "Geriatric Use" subsection to the **PRECAUTIONS** section of the labeling in compliance with 21 CFR 201.57(f)(10). Supplement 005 provides for updated pharmacokinetic information regarding the impact of gender and hepatic dysfunction to the **CLINICAL PHARMACOLOGY section, Special Populations subsection and** to the **DOSAGE AND ADMINISTRATION** section. We note that these supplements are superseded by S-006; therefore, these supplements will be Acknowledged and Retained in our files.

Supplement 006 provides support for conversion of ZINECARD™ for Injection (dexrazoxane for injection) from accelerated to regular approval.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling text for the package insert.

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 ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-212/S-006." Approval of this submission by FDA is not required before the labeling is used.

We approved this NDA under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of this supplement fulfills your commitments made under 21 CFR 314.510.

We recommend that you conduct a clinical study to characterize the pharmacokinetics of dexrazoxane in Asian females. In your study that assessed the pharmacokinetics of males and females, the two Asian women had high dexrazoxane clearances, almost twice the mean values in Caucasian females.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division/ the Division of Oncology Drug Products and two copies of both the promotional materials and the package insert(s) directly to:

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

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, HF-2
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 Brenda Atkins, Regulatory Project Manager, at (301) 594-5767.

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

Enclosure: Labeling – 10 pages

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

/s/

Grant Williams
10/31/02 05:51:21 PM
For Richard Pazdur