



NDA 50-778/S-003/S-004

Pharmacia & Upjohn Company
Mail Stop 0200-298-113
7000 Portage Road
Kalamazoo, MI 49001-0199

Attention: Gregory A. Brier
Senior Regulatory Manager

Dear Mr. Brier:

Please refer to your supplemental new drug applications dated April 20, 2001 (S-003) and November 16, 2002 (S-004), received April 23, 2001 and November 19, 2001 respectively, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for ELLENCE® (epirubicin hydrochloride injection) 50 mg/25 mL and 200 mg/100 mL single-use vials. We also refer to your submission containing final printed labeling (FPL) and immediate container and carton labels submitted September 30, 1999 in response to our September 15, 1999 approval letter for this NDA.

We acknowledge receipt of your submission dated October 30, 2002 amending S-004.

These "Changes Being Effected" supplemental new drug applications provide for strengthening the safety information, to correct and round hazard ratios, and to revise information for administration and length of infusion time for ELLENCE® in the FPL.

We have completed the review of these supplemental new drug applications and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted draft labeling on October 30, 2002. Accordingly, the supplemental new drug application S-004 is approved effective on the date of this letter.

However, please note the following editorial revision listed below, which should be included in the FPL.

The **DOSAGE AND ADMINISTRATION, Preparation & Administration Precautions** section should include a statement "Procedures normally used for proper handling and disposal of anti-cancer drugs should be considered for use with ELLENCE. Several guidelines on this subject have been published¹⁻⁸." A **REFERENCES** section should be added to the PI listing the following:

1. ONS Clinical Practice Committee. Cancer Chemotherapy Guidelines and Recommendations for Practice. Pittsburgh, Pa: Oncology Nursing Society; 1999:32-41.

2. Recommendations for the Safe Handling of Parenteral Antineoplastic Drugs. Washington, DC: Division of Safety, Clinical Center Pharmacy Department and Cancer Nursing Services, National Institutes of Health; 1992. US Dept of Health and Human Services, Public Health Service Publication NIH 92-2621.
3. AMA Council on Scientific Affairs. Guidelines for Handling Parenteral Antineoplastics. *JAMA*. 1985;253:1590-1591.
4. National Study Commission on Cytotoxic Exposure – Recommendations for Handling Cytotoxic Agents. 1987. Available from Louis P. Jeffrey, Sc.D., Chairman, National Study Commission on Cytotoxic Exposure. Massachusetts College of Pharmacy and Allied Health Sciences, 179 Longwood Avenue, Boston, MA 02115.
5. Clinical Oncological Society of Australia. Guidelines and Recommendations for Safe Handling of Antineoplastic Agents. *Med J Australia*. 1983;1:426-428.
6. Jones RB, Frank R, Mass T. Safe Handling of Chemotherapeutic Agents: A Report from the Mount Sinai Medical Center. *CA-A Cancer J for Clin*. 1983;33:258-263.
7. American Society of Hospital Pharmacists. ASHP Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs. *Am J Hosp Pharm*. 1990;47:1033-1049.
8. Controlling Occupational Exposure to Hazardous Drugs. (OSHA Work-Practice Guidelines). *Am J Health-Syst Pharm*. 1996;53:1669-1685.

We also note that S-004 supersedes both the FPL submitted September 30, 1999 and supplement S-003 submitted April 20, 2001. Therefore, these documents will be retained in our files.

The final printed labeling (FPL) must be identical to the proposed package insert submitted October 30, 2002 (copy code 817 911 104) dated January 2002 with the editorial revision indicated above. These revisions are terms of the approval of S-004.

Please submit the copies of final printed labeling (FPL) electronically to your application 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 heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 50-778/S-004." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a “Dear Health Care Practitioner” 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

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, call Brenda Atkins, Consumer Safety Officer, 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

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

/s/

Richard Pazdur
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