DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-297/S-025, S-026, S-027

Serono, Inc.
Attention: Pamela Williamson Joyce
Vice President, Regulatory Affairs, North America
One Technology Place
Rockland, MA 02370

Dear Ms. Joyce:

Please refer to your supplemental new drug applications dated May 15, 2002, received May 16, 2002, July 3, 2002, received July 5, 2002, and October 7, 2002, received October 8, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Novantrone® (mitoxantrone for injection concentrate).

The supplemental 025 new drug application is a "Changes Being Effected" which provides for additional information regarding signs and symptoms of extravasation, as well as methods for administration based on 8 post-marketing reports of extravasation received for patients receiving NOVANTRONE for Multiple Sclerosis.

The supplemental 026 new drug application is a "Prior Approval" which provides for proposed text for the Geriatric Use Labeling. In addition, this supplement contains proposed changes to the Clinical Pharmacology section.

The supplemental 027 new drug application is a "Changes Being Effected" which provides additional information regarding acute myelogenous leukemia (AML) in the warning sections. This revision is based on 5 MedWatch reports for patients receiving NOVANTRONE for Multiple Sclerosis and includes the supplement 025 revisions.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the supplemental 025 application is acknowledged and retained and supplemental 026 and 027 are approved effective on the date of this letter.

The final printed labeling (FPL) must incorporate the S-026 submitted draft labeling (package insert submitted July 3, 2002) changes into the S-027 submitted draft labeling (package insert submitted October 7, 2002). The FPL should also include the References revision noted below.

It is the policy of the Office of Drug Evaluation I and the Division of Oncology Drug Products to include only those references, which pertain to the handling of antineoplastic agents. Therefore, we recommend you to add the following reference and renumber the remaining references appropriately. This may be implemented at the next printing.

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

Please 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. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved supplement NDA 19-297/S-027." 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 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

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

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

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/s/

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Richard Pazdur

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