DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-297/S-030 and S-031

EMD Serono, Inc.
One Technology Place
Rockland, MA 02370

Attention: Jill P. Hillier, Ph.D.
Director, Global Regulatory Affairs

Dear Dr. Hillier:

Please refer to your supplemental new drug applications dated August 28 and October 2, 2008, received August 28 and October 2, 2008, respectively, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Novantrone® (mitoxantrone HCl) Injection.

We acknowledge receipt of your submissions dated December 15, 2008.

These "Changes Being Effected" supplemental new drug applications provide for updates and clarifications to the **Boxed Warning** and **Warnings** sections of the package insert, revisions to the **Patient Information Leaflet**, addition of Tall Man lettering to the package insert, patient information leaflet and product packaging, and revised placement of the concentration on the product packaging.

We completed our review of these applications. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions listed below.

- At the time of the next printing, please revise the References section to remove the following out-of-date reference:

  NIH [2002]. 1999 recommendations for the safe handling of cytotoxic drugs. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, NIH Publication No. 92-2621.

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the submitted labeling (package insert, patient package insert, immediate container and carton labels submitted October 2, 2008), and should also reflect the following revisions as agreed upon in your December 15, 2008, correspondence:

- In the Patient Information Sheet, under the "**What diagnostic tests will be performed?**" section, please revise the third paragraph as follows (additions shown as <u>underlined</u> text):

  "To measure possible changes to the heart, <u>you should have regular electrocardiograms (ECGs)</u>

and you should have regular testing of your heart's ability to pump blood. Measuring your heart's ability to pump blood requires taking pictures of your heart using a simple, painless test such as an echocardiogram. Your heart should be tested before each dose of NOVANTRONE, or if you show signs of heart problems."

- In the Patient Information Sheet, under the "**What are the possible side effects of NOVANTRONE?**" section, please edit the last sentence of paragraph one as follows (additions shown as underlined text):

  "These problems generally happen in people who get a total lifetime dose of more than 12 doses (usually more than 140 mg/m2) of NOVANTRONE, but can also occur at lower lifetime doses.

- On the carton and container labels, replace the words "in" and "per" with a slash mark "/" in the expression of strength to be in accordance with USP General Requirements for Labels and Labeling of Injectable Drug Products. Revise to read as follows on the label and labeling:

  20 mg/10 mL
  (2 mg/mL)

- Your label and labeling indicate the product is a multidose. This terminology leads healthcare practitioners to believe the product can be used multiple times for a number of days (e.g., 30 days). However, once entered your product is stable for only 7 days at room temperature and 14 days under refrigeration. Thus, we request you include a concise statement for the expiration for the drug product after initial use on the side or principal display panel of the container label and carton labeling. This will minimize the use of the product beyond 7 or 14 days.

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil.spl.html that is identical to the enclosed labeling (text for package insert, patient package insert). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 19-297/S-030 and S-031."

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
Food and Drug Administration
Suite 12B05
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 Diane Hanner, Regulatory Project Manager, at (301) 796-4058.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D.
Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure

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

/s/

Robert Justice

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