CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-277

OTHER ACTION LETTER(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-277

COMPLETE RESPONSE

Schering Corporation
Attention: Marion Ceruzzi, Ph.D.
Senior Manager, Global Regulatory Affairs
2000 Galloping Hill Road
Kenilworth, NJ 07033

Dear Dr. Ceruzzi:

Please refer to your new drug application (NDA) dated January 23, 2008, received January 24, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Temodar (temozolomide) for Injection 100 mg/vial.

We acknowledge receipt of your submissions dated May 16, 22, August 22, September 24, October 2, 16, 17, November 4 and 14, 2008.

We have completed the review of your application, as amended, and have determined that we cannot approve this application in its present form. We have described below our reasons for this action and, where possible, our recommendations to address these issues.

During a recent inspection of the Schering Plough (Brinny) Co. manufacturing facility for this application, our field investigator conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.

Additional information is needed to address several issues pertinent to clarifying the safety or efficacy of this product. We request that you propose studies and/or clinical trials, or include this information in your Complete Response, to address the following issues:

> Perform a rodent bridging study comparing the toxicity of temozolomide alone with temozolomide spiked with **(b) (4)** . The study should mimic a single cycle of the approved clinical schedule (intravenously daily x 5 every 28 days) and utilize concentrations of **(b) (4)** which exceed **(b) (4)** respectively, to adequately qualify these impurities at levels proposed in the current specifications for drug substance and drug product.

Describe your plans to address the above issues in sufficient detail to permit our evaluation of the adequacy of the proposals. Your response should include:

- A detailed protocol or, at a minimum, a detailed outline describing all design features of the study/clinical trial including sample size and justification, eligibility criteria with rationale, dosing regimens and duration, clinical assessments to be performed and their timing, and endpoints to be analyzed.

- Alternatively, the final report may be included in your resubmission.

Submit draft labeling that incorporates agreed upon revisions in the attached labeling. In addition, submit updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html.

Within one year after the date of this letter, you are required to resubmit or take one of the other actions available under 21 CFR 314.110. If you do not take one of these actions, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the FDA Guidance for Industry *Formal Meetings With Sponsors and Applicants for PDUFA Products*, February, 2000 (http://www.fda.gov/cder/guidance/2125fnl.htm).

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call Paul Zimmerman, Regulatory Project Manager, at 301-796-1489.

Sincerely,

{See appended electronic signature page}

Robert Justice, MD
Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Office of New Drugs
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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