DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-029

Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Attention: Joseph F. Lamendola, Ph.D.
Vice President
U.S. Regulatory Affairs

Dear Dr. Lamendola:

Reference is made to your correspondence dated April 27, 2001, requesting changes to FDA's January 25, 2001, Written Request for pediatric studies for Temodar® (temozolomide) Capsules.

We have reviewed your proposed changes and are amending the below listed sections of the Written Request. All other terms stated in our Written Request issued on January 25, 2001 remain the same.

Types of studies:

Phase 1: A dose finding study, including pharmacokinetics, with doses determined for all appropriate age groups. The number of patients entered should be sufficient to achieve Phase 1 objectives, which may be in the range of 18-25.

Phase 2 or pilot studies: Enrollment of at least 14 pediatric patients each with refractory or relapsed tumors. Studies should be performed at facilities that have the experience, support, and expertise to care for children with cancer.

changed to:

Phase 1: A summary report of the Phase 1 information in pediatric subjects (data previously submitted to the NDA). This report will include pharmacokinetics and dose determination in more than 18 subjects covering the age group described above.

Phase 2 or pilot studies: Enrollment of more than 14 patients with recurrent Central Nervous System (CNS) tumors, in each to the two following studies: a two-arm Phase 2 study and a six-arm Phase 2 pilot study. The tumor histologies covered by these two studies are to include:

- High grade astrocytoma (Grade 3 and 4 astrocytoma, glioblastoma multforme, anaplastic astrocytoma)
- Brain stem glioma
- Low grade astrocytoma (Grade 1 and 2 astrocytoma, pilocytic astrocytoma)
- Ependymoma

- Medulloblastoma/Primitive Neuroectodermal Tumor (PNET)
- Other CNS tumors-to be described in each report.

The studies should be performed at facilities that have the experience, support, and expertise to care for children with cancer.

Age group in which study(ies) will be performed:

Infants > 1 month to adolescents

changed to:

3 years to 17 years

Format of reports to be submitted:

Full study reports not previously submitted to the Agency addressing the issues outlined in this request with full analysis, assessment, and interpretation.

changed to:

A summary of the Phase 1 study. Complete study reports addressing the issues outlined in this request for the Phase 2 or pilot studies. In addition to narrative sections, these reports should provide patient line listings that include, but are not limited to, drug exposure, diagnosis, prior therapy, tumor measurement, and all adverse events whether drug related or not, as well as descriptive statistics.

Reports of the studies that meet the terms of the Written Request dated January 25, 2001, as amended by this letter must be submitted to the Agency on or before December 31, 2002, in order to possibly qualify for pediatric exclusivity extension under Section 505A of the Act.

Please submit protocols for the above studies to an investigational new drug application (IND) and clearly mark your submission, "PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY" in large font, bolded type at the beginning of the cover letter of the submission. Please notify us as soon as possible if you wish to enter into a written agreement by submitting a proposed written agreement. Please clearly mark your submission, "PROPOSED WRITTEN AGREEMENT FOR PEDIATRIC STUDIES" in large font, bolded type at the beginning of the cover letter of the submission.

Reports of the studies should be submitted as a SUPPLEMENT TO YOUR APPROVED NDA with the proposed labeling changes you believe would be warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "SUBMISSION OF PEDIATRIC STUDY REPORTS - PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED" in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. Please also send a copy of the cover letter of your submission, via fax (301-594-0183) or messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North 11, 7500 Standish Place, Rockville, MD 20855-2773.

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked "PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES" in large font, bolded type at the beginning of the cover letter of the submission. You will be notified in writing if any changes to this Written Request are agreed upon by the Agency.

We hope you will fulfill this pediatric study request. We look forward to working with you on this matter in order to develop additional pediatric information that may produce health benefits to the pediatric population.

If you have any questions, contact Sean Bradley, R.Ph., Regulatory Project Manager, at 301-594-5750.

Sincerely,

{See appended electronic signature page}

Rachel E. Behrman, M.D., M.P.H.
Deputy Director
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/

Robert Temple

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