DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA: 20-363

Novartis Pharmaceuticals Corporation
Attention: James L. DeMartino, Ph.D.,
Associate Director, Drug Regulatory Affairs
59 Route 10
East Hanover, New Jersey 07936-1080

Dear Dr. DeMartino:

To obtain needed pediatric information on famciclovir, the Food and Drug Administration (FDA) is hereby making a formal Written Request, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic Act (the Act), that you submit information from the following studies:

Type of studies:
Study #1: A single-dose pharmacokinetic study in infants and children age one month to five years who are receiving suppressive therapy for recurrent episodes of central nervous system (CNS) or skin-eye-mouth disease due to neonatal herpes simplex virus (HSV) infection.

Study #2: A single-dose pharmacokinetic study in immunocompetent and/or immunocompromised infants and children age one to twelve years who have HSV infections.

Study #3: A single-dose pharmacokinetic study in immunocompetent and/or immunocompromised infants and children age one to twelve years who have varicella zoster virus (VZV) infections.

Age-appropriate safety data should be collected for Studies 1, 2, and 3.

Age group in which studies will be performed:
Study #1: An adequate number of patients should be included to support dosing in each of the following age groups: 1 - 6 months, 6 months - 1 year, 1 year – 2 years, and 2 - 5 years.

Study #2: An adequate number of patients should be included to support dosing for HSV in infants and children ages 1 - 2 years and 2 - 12 years.

Study #3: An adequate number of patients should be included to support dosing for VZV in infants and children ages 1 - 2 years and 2 - 12 years.

Study Endpoints for Studies #1, 2, 3:
Pharmacokinetics parameters such as Cmax, Cmin, Tmax, t1/2, AUC, and Cl/F.

Drug Information:
Dosage form: age-appropriate dosage form.
Route of administration: oral
Regimen: to be determined by development program.

Drug specific safety concerns:
Neutropenia, CNS toxicity, nausea, vomiting, diarrhea and increased transaminases.

Statistical information, including power of study and statistical assessments
Studies #1, 2, and 3:

- Descriptive analyses of pharmacokinetic parameters.
- Descriptive analyses of reported adverse events.
- Studies should include an adequate number of patients to characterize pharmacokinetics over the age range studied, taking into account inter-subject and intra-subject variability. The number of patients should be uniformly distributed across the age range studied.

Labeling that may result from these studies:
Information regarding the pharmacokinetics and safety of famciclovir in the pediatric population.

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. Please include other information as appropriate.

Timeframe for submitting reports of the studies:
Reports of the above studies must be submitted to the Agency on or before December 31, 2003. Please remember that pediatric exclusivity extends only existing patent protection or exclusivity that has not expired or been previously extended at the time you submit your reports of the studies in response to this Written Request.

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. 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 new drug application or 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 facsimile (301) 594-0183 or messenger to the

Director, Office of Generic Drugs, HFD-600, Metro Park North II, 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 in the pediatric population.

If you have any questions, please contact Sean R. Byrd, Regulatory Project Manager, at (301) 827-2335.

Sincerely yours,

M. Dianne Murphy, M.D.
Director
Office of Drug Evaluation IV
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/

Dianne Murphy
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