



NDA 20-550

GlaxoSmithKline
Attention: Sherman N. Alfors
Project Director, Regulatory Affairs
Five Moore Drive
Research Triangle Park, NC 27709

Dear Mr. Alfors:

To obtain needed pediatric information on valacyclovir hydrochloride, the Food and Drug Administration is hereby making a formal Written Request, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic 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 C_{max}, C_{min}, T_{max}, t_{1/2}, AUC, and CI/F.

Drug Information:

Dosage form: age-appropriate dosage form.

Route of administration: oral

Regimen: to be determined by development program.

Drug specific safety concerns:

Renal toxicity (precipitation of acyclovir in renal tubules), neutropenia, CNS toxicity, and thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS) in immunocompromised patients.

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

- Descriptive analyses of pharmacokinetic parameters.
- Descriptive analyses of reports of 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 valacyclovir 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 Karen A. Young, RN, BSN, 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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