NDA 20-363/SLR-019

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

27 MAR 2001

Dear Dr. DeMartino:

Please refer to your Labeling Supplement-Changes Being Effected, dated August 29, 2000, received August 30, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Famvir® (famciclovir) Tablets.

In this Labeling Supplement-Changes Being Effected (SLR-019), you submitted the following wording for the "Drug Resistance" subsection in the **MICROBIOLOGY** section of the Famvir® label:

> "Resistance of HSV and VZV to antiviral nucleoside analogs can result from mutations in the viral thymidine kinase (TK) and DNA polymerase genes. Mutations in the viral TK gene may lead to complete loss of viral TK activity (TK negative), reduced levels of TK activity (TK partial), or alteration in the ability of viral TK to phosphorylate the drug without an equivalent loss in the ability to phosphorylate thymidine (TK altered). The most commonly encountered acyclovir-resistant mutants are TK negative and they are also resistant to penciclovir."

In your next printing of the Famvir® label, please revise the complete "Drug Resistance" subsection in the **MICROBIOLOGY** section of the Famvir® label to read as follows:

> "Penciclovir-resistant mutants of HSV and VZV can result from mutations in the viral thymidine kinase (TK) and DNA polymerase genes. Mutations in the viral TK gene may lead to complete loss of TK activity (TK negative), reduced levels of TK activity (TK partial), or alteration in the ability of viral TK to phosphorylate the drug without an equivalent loss in the ability to phosphorylate thymidine (TK altered). The most commonly encountered acyclovir-resistant mutants that are TK negative are also resistant to penciclovir. The possibility of viral resistance to penciclovir should be considered in patients who fail to respond or experience recurrent viral shedding during therapy."

We have completed review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the agreed upon labeling text. Accordingly, this supplemental application is approved effective on the date of this letter, provided that the above-mentioned changes are made at the time of the next Famvir® label printing.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact Virginia L. Yoerg, Regulatory Project Manager, at (301) 827-2335.

Sincerely,

Debra B. Birnkrant, M.D.
Acting Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

/s/

Debra Birnkrant
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