CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 74976

ADMINISTRATIVE DOCUMENTS

ANDA APPROVAL SUMMARY

ANDA: 74-976 DRUG PRODUCT: Acyclovir DOSAGE FORM: Tablet

FIRM: Genpharm Inc. STRENGTH: 400 mg & 800 mg

CGMP STATEMENT/EIR UPDATE STATUS: Acceptable for all on 5/27/97.

BIO STUDY: The *in vivo* bioequivalence study for 800 mg tablet (Lot #102394) found acceptable, waiver for bioequivalence study requirements for 400 mg tablet granted, and dissolution testing for 400 mg tablet (Lot #102393) and 800 mg tablet (Lot #102394) found acceptable on 10/5/97 by Andre Jackson.

VALIDATION -(DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):
Active Ingredient: N/A, product is compendial refer to memo dated 11/14/90 regarding Compliance Program Guidance Manual # 7346.832, code 52832 for ANDAs and AADAs.
*** Finish Dosage Form: **Sent to St. Louis on 10/23/97.**

STABILITY - ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION?:
Protocol: Satisfactory
Exp.Date: 24 months - 40°C, 75% R.H., 3 months and R.T. (25°C, 60% R.H.), 3 months, smallest and largest container/closure system, 1 lot each strength.
Container/Closure systems are the same.

LABELING: Container: Satisfactory in FPL.
UD Carton: Satisfactory in FPL.
UD Blister: Satisfactory in FPL.
Insert: Satisfactory in FPL.

SIZE OF BIO BATCH (FIRM'S SOURCE OF NDS OK?):
units of 400 mg tablets Lot #102393) and units of 800 mg tablets Lot #102394), source of NDS acceptable

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH, WERE THEY MANUFACTURED VIA THE SAME PROCESS?):
units of 400 mg tablets Lot #102393) and units of 800 mg tablets , Lot #102394).

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?:
units of 400 mg tablets and units of 800 mg

1/27/98

CHEMIST: Norman Gregory DATE: 1/6/98

SUPERVISOR: U.V. Venkataram, Ph.D. DATE: 1/14/98

1/29/98

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 74-976 Date of Submission: October 1, 1997

Applicant's Name: Genpharm Inc.

Established Name: Acyclovir Tablets, 400 mg and 800 mg

Labeling Deficiencies:

1. GENERAL COMMENT

   Since this ANDA shares an insert with ANDA 74-977, Acyclovir Capsules, both applications must be approved together or you will be asked to further revise the insert.

2. INSERT

   a. GENERAL COMMENT

      You may decrease the prominence of "ACYCLOVIR" throughout the text by using lower case letters since this is not a proprietary name as is ZOVIRAX®.

   b. DESCRIPTION

      Your components and composition statement mentions that the product contains FD & C Yellow No. 10 Aluminum Lake while the insert mentions D & C Yellow No. 10 Aluminum Lake. Please comment and/or revise.

   c. PRECAUTIONS

      i. Carcinogenesis, Mutagenesis, Impairment of Fertility

         A). First paragraph, last sentence

            ... (see CLINICAL PHARMACOLOGY, Pharmacokinetics).

B). Third paragraph, last sentence

... in five *in vitro* ... ("five" rather than "live")

C). Fourth paragraph, first sentence

A positive result ... weanling mice. ("result" and "weanling" rather than "results" and "weaning").

ii. Pregnancy: *Teratogenic Effects:*

Include the following text at the end of the second paragraph:

... women. A prospective epidemiological registry of acyclovir use during pregnancy has been ongoing since 1984. As of June 1996, outcomes of live births have been documented in 494 women exposed to systemic acyclovir during the first trimester of pregnancy. The occurrence rate of birth defects approximates that found in the general population. However, the small size of the registry is insufficient to evaluate the risk for less common defects or to permit reliable and definitive conclusions regarding the safety of acyclovir in pregnant women and their developing fetuses. Acyclovir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

d. DOSAGE AND ADMINISTRATION

i. Genital Herpes - Chronic Suppressive Therapy for Recurrent Disease

The sentence beginning "The frequency and ..." should begin a new paragraph

ii. Treatment of Chickenpox - Children (2 years of age and older)

20 mg/kg per dose orally four times daily (80 mg/kg/day) ...

iii. Include the following subsection as the last subsection in this section:

Bioequivalence of Dosage Forms: Acyclovir suspension was shown to be bioequivalent to acyclovir capsules (n=20) and one acyclovir 800 mg tablet was shown to be bioequivalent to four acyclovir 200 mg capsules (n=24).

Please revise your package insert labeling, as instructed above, and submit in final print.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research