

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER      74976**

**ADMINISTRATIVE DOCUMENTS**

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

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ANDA Number: 74-977 Date of Submission: October 1, 1997

Applicant's Name: Genpharm Inc

Established Name: Acyclovir Capsules 200 mg

Labeling Deficiencies:

1. GENERAL COMMENT

Since this ANDA shares an insert with ANDA 74-976, Acyclovir Tablets, 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

- i. Revise "corn starch" to read "pregelatinized starch".
- ii. 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) ...

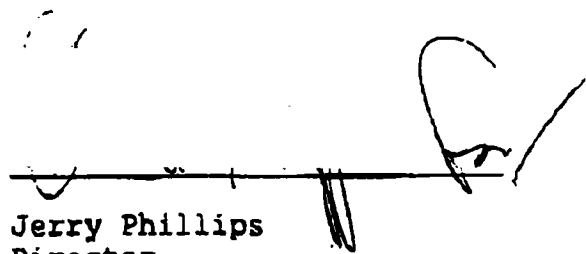
- iii. Include the following subsection as the last subsection in this section:

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.



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

✓

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

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**ANDA Number:** 74-977

**Date of Submission:** September 27, 1996

**Applicant's Name:** Genpharm Inc.

**Established Name:** Acyclovir Capsules, 200 mg

**Labeling Deficiencies:**

1. **CONTAINER:**
  - a. **General Comment**  

We encourage you to differentiate between the container labels for your 200 mg capsule dosage form and your 400 mg and 800 mg tablet dosage forms, [the subject of ANDA 74-976] by using boxing and/or contrasting colors.
  - b. **200 mg (100s)**
    - i. Immediately beneath the established name delete "(Acyclovir)".
    - ii. Relocate the tablet strength to immediately follow the established name and delete "Each tablet contains \_\_\_\_".
  - c. **200 mg (unit dose blister)**
    - i. Revise "capsules" to read "capsule".
    - ii. See comments b(i) and b(ii).
2. **CARTON: 200 mg (unit-dose 100s)**
  - a. See comments 1(b)(i) and 1(b)(ii) under CONTAINER.
  - b. Include a statement as to whether or not the unit-dose package is child-resistant. If it is not child-resistant, we encourage the inclusion of a statement that if dispensed to outpatients, it should be with a child resistant container. We suggest the following text:

This unit-dose package is not child-resistant. If dispensed for outpatient use, a child-resistant container should be utilized.

[Note: The second sentence is optional.]

3. INSERT

a. General Comment

- i. When abbreviating micrograms we encourage the use of "mcg" rather than "µg". Please revise your insert labeling accordingly.
- ii. Please refer to the enclosed mocked-up copy of your draft insert labeling for further revisions.

b. DESCRIPTION

- i. Revise the first sentence to read, "Acyclovir is an antiviral drug".
- ii. Include the dyes in the imprinting ink in the list of inactive ingredients.
- iii. Please note there are now two official monographs for lactose listed in USP 23/NF 18. Revise "lactose" to read "lactose monohydrate".
- iv. Include the chemical formula:  
$$C_8H_{11}N_5O_3$$
- v. To be in accord with USP 23, make the following revisions in the last paragraph:  
...a white to off-white crystalline powder with a molecular weight of 225.21, and ...

c. CLINICAL PHARMACOLOGY (Pharmacokinetics) -

- i. Delete the first sentence of the third paragraph, "A single ... solution" and revise the last sentence to read, "In a reported single-dose bioavailability/bioequivalence study in 24 volunteers, ..."
- ii. Revise the fifth paragraph to read:  
In another study the influence of food ...

d. **INDICATIONS AND USAGE (Chickenpox)**

In the first sentence of the first and second paragraphs print "with 24 hours" in bold print.

e. **PRECAUTIONS**

i. **Information for Patients (Genital Herpes Infections)**

Second paragraph, last sentence -

... number of chromosomes.<sup>28</sup>  
["28" instead of "29"]

ii. **Pediatric Use**

... in pediatric patients less ...

f. **ADVERSE REACTIONS (Observed During Clinical Practice)**

*Nervous*

...paresthesia, seizure, somnolence...  
[Add "seizure"].

g. **HOW SUPPLIED**

We encourage you to include the following statement at the end of this section, "CAUTION: Federal law prohibits dispensing without prescription".

h. **REFERENCES**

Revise as follows:

- i. 4. Furman PA, ...
- ii. 7. ... In: Turner [add space] ...ed 3. [add period] ... Livingstone; 1983: [add space] ...
- iii. 17. ... *Am J Med*.... [italic print]
- iv. 18. ... *N Engl J Med* ... [italic print]
- v. 27. ... *Lancet* ... [italic print]
- vi. 37. ... Rotbart HA, ...





suppressive therapy. Some patients, such as those with very frequent or severe episodes before treatment, may warrant uninterrupted suppression for more than a year.

Chronic suppressive therapy is most appropriate when, in the judgement of the physician, the benefits of such a regimen outweigh known or potential adverse effects. In general, orally administered Acyclovir should not be used for the suppression of recurrent disease in mildly affected patients. Unanswered questions concerning the relevance to humans of *in vitro* mutagenicity studies and reproductive toxicity studies in animals given high parenteral doses of acyclovir for short periods (see PRECAUTIONS: Carcinogenesis, Mutagenesis, Impairment of Fertility) should become in mind when designing long-term management for individual patients. Discussion of these issues with patients will provide them the opportunity to weigh the potential for toxicity against the severity of their disease. Thus this regimen should be considered only for appropriate patients with annual re-evaluation.

Limited studies<sup>31,32</sup> have shown that there are certain patients for whom intermittent short-term treatment of recurrent episodes is effective. This approach may be more appropriate than a suppressive regimen in patients with infrequent recurrences.

Immunocompromised patients with recurrent herpes infections can be treated with either intermittent or chronic suppressive therapy. Clinically significant resistance, although rare, is more likely to be seen with prolonged or repeated therapy in severely immunocompromised patients with active lesions.

#### **Herpes Zoster Infections:**

In a double-blind, placebo-controlled study of 187 normal patients with localized cutaneous zoster infection (93 randomized to Acyclovir and 94 to placebo). Acyclovir (800 mg 5 times daily for 10 days) shortened the times to lesion scabbing, healing and complete cessation of pain, and reduced the duration of viral shedding and the duration of new lesion formation.<sup>33</sup>

In a similar double-blind, placebo-controlled study in 83 normal patients with herpes zoster (40 randomized to Acyclovir and 43 to placebo), Acyclovir (800 mg 5 times daily for 7 days) shortened the times to complete lesion scabbing, healing and cessation of pain, reduced the duration of new lesion formation and reduced prevalence of localized zoster-associated neurologic symptoms (paresthesia, dysesthesia or hyperesthesia).<sup>34</sup>

#### **Chickenpox:**

In a double-blind, placebo-controlled efficacy study in 110 normal patients, ages 5 to 16 years, who presented within 24 hours of the onset of a typical chickenpox rash, Acyclovir was administered orally 4 times daily for 5 to 7 days at doses of 10, 15 or 20 mg/kg depending on the age group. Treatment with Acyclovir reduced the maximum number of lesions (336 vs. greater than 500; lesions beyond 500 were not counted). Treatment with Acyclovir also shortened the mean time to 50% healing (7.1 days vs. 8.7 days), reduced the number of vesicular lesions by the second day of treatment (49 vs. 113), and decreased the proportion of patients with fever (temperature greater than 100°F) by the second day (19% vs. 57%). Treatment with Acyclovir did affect the antibody response to varicella-zoster virus measured 1 month and 1 year following the treatment.<sup>35</sup>

orally 6 times a day (dosing appropriate for treatment of genital herpes). Plasma drug concentrations in animal studies are expressed as multiples of human exposure to acyclovir at the higher and lower dosing schedules (see Pharmacokinetics).

CLINICAL PHARMACOLOGY

Acyclovir was tested in lifetime bioassays in rats and mice at single daily doses of up to 450 mg/kg administered by gavage. There was no statistically significant difference in the incidence of tumors between treated and control animals, nor did acyclovir shorten the latency of tumors. At 450 mg/kg/day, plasma concentrations were 3 to 6 times human levels in the mouse bioassay and 1 to 2 times human levels in the rat bioassay.

Acyclovir was tested in two *in vitro* cell transformation assays. Positive results were observed at the highest concentration tested (31 to 63 times human levels) in one system and the resulting morphologically transformed cells formed tumors when inoculated into immunosuppressed, syngeneic, weaning mice. Acyclovir was negative (40 to 80 times human levels) in the other, possibly less sensitive, transformation assay.

In acute cytogenetic studies, there was an increase, though not statistically significant, in the incidence of chromosomal damage at maximum tolerated parenteral doses of acyclovir (100 mg/kg) in rats (62 to 125 times human levels) but not in Chinese hamsters; higher doses of 500 and 1000 mg/kg were clastogenic in Chinese hamsters (380 to 760 times human levels). In addition, no activity was found after 5 days dosing in a dominant lethal study in mice (36 to 73 times human levels). In all 4 microbial assays, no evidence of mutagenicity was observed. Positive results were obtained in 2 of 7 genetic toxicity assays using mammalian cells *in vitro* in human lymphocytes a positive response for chromosomal damage was seen at concentrations 150 to 300 times the acyclovir plasma levels achieved in humans. At one locus in mouse lymphoma cells, mutagenicity was observed at concentrations 250 to 500 times human plasma levels. Results in the other five mammalian cell loci follow at 3 loci in a Chinese hamster ovary cell line, the results were inconclusive at concentrations at least 1850 times human levels at 2 other loci in mouse lymphoma cells, no evidence of mutagenicity was observed at concentrations at least 1500 times human levels.

Acyclovir has not been shown to impair fertility or reproduction in mice (450 mg/kg/day, p.o.) or in rats (25 mg/kg/day, s.c.). In the mouse study, plasma levels were 9 to 18 times human levels while in the rat study they were 8 to 15 times human levels. At a higher dose in the rat (50 mg/kg/day, s.c.), there was a statistically significant increase in post-implantation loss, but no concomitant decrease in litter size. In female rabbits treated subcutaneously with acyclovir subsequent to mating, there was a statistically significant decrease in implantation efficiency but no concomitant decrease in litter size at a dose of 50 mg/kg/day (16 to 31 times human levels). No effect upon implantation efficiency was observed when the same dose was administered intravenously (53 to 106 times human levels). In a rat peri- and postnatal study at 50 mg/kg/day s.c. (11 to 22 times human levels), there was a statistically significant decrease in the group mean numbers of corpora lutea, total implantation sites, and live fetuses in the F<sub>2</sub> generation. Although not statistically significant, there was also a dose-related decrease in group mean numbers of live fetuses and implantation sites at 12.5 mg/kg/day and 25 mg/kg/day s.c. The intravenous administration of 100 mg/kg/day, a dose known to cause obstructive nephropathy in rabbits, caused a significant increase in fetal resorptions and a corresponding decrease in litter size (plasma levels

commonly stated as period

were not measured). However, at a maximum tolerated intravenous dose of 50 mg/kg/day in rabbits (53 to 106 times human levels), no drug-related reproductive effects were observed.

Intraperitoneal doses of 80 or 320 mg/kg/day acyclovir given to rats for 6 and 1 months, respectively, caused testicular atrophy. Plasma levels were not measured in the 1-month study and were 24 to 48 times human levels in the 6-month study. Testicular atrophy was persistent through the 4-week postdose recovery phase after 320 mg/kg/day; some evidence of recovery of sperm production was evident 30 days postdose. Intravenous doses of 100 and 200 mg/kg/day acyclovir given to dogs for 31 days caused aspermatogenesis. At 100 mg/kg/day plasma levels were 47 to 94 times human levels, while at 200 mg/kg/day they were 159 to 317 times. No testicular abnormalities were seen in dogs given 50 mg/kg/day i.v. for 1 month (21 to 41 times human levels) and in dogs given 60mg/kg/day orally for 1 year (6 to 12 times human levels).

abnormalities

**Pregnancy: Teratogenic Effects:** Pregnancy Category C Acyclovir was not teratogenic in the mouse (450 mg/kg/day, p.o.) rabbit (50 mg/kg/day, s.c. and i.v.) or in standard tests in the rat (50 mg/kg/day, s.c.). These exposures resulted in plasma levels 9 and 18, 16 and 106, and 11 and 22 times, respectively, human levels in a non-standard test in rats, there were fetal abnormalities, such as head and tail anomalies and maternal toxicity.<sup>42</sup> In this test, rats were given 3 s.c. doses of 100 mg/kg acyclovir on gestation day 10, resulting in plasma levels 63 and 125 times human levels. There are no adequate and well-controlled studies in pregnant women. Acyclovir should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. Although acyclovir was not teratogenic in standard animal studies, the drug's potential for causing chromosome breaks at high concentration should be taken into consideration in making this determination.

**Nursing Mothers:** Acyclovir concentrations have been documented in breast milk in two women following oral administration of Acyclovir and ranged from 0.6 to 4.1 times corresponding plasma levels.<sup>43,44</sup> These concentrations would potentially expose the nursing infant to a dose of acyclovir up to 0.3 mg/kg/day. Caution should be exercised when Acyclovir is administered to a nursing woman.

**Pediatric Use:** Safety and effectiveness in children less than 2 years of age have not been adequately studied.

#### ADVERSE REACTIONS:

**Herpes Simplex: Short-Term Administration:** The most frequent adverse events reported during clinical trials of treatment of genital herpes with orally administered Acyclovir were nausea and/or vomiting in 8 of 298 patient treatments (2.7%) and headache in 2 of 298 (0.6%). Nausea and/or vomiting occurred in 2 of 287 (0.7%) patients who received placebo.

Less frequent adverse events, each of which occurred in 1 of 298 patient treatments with orally administered Acyclovir (0.3%), included diarrhea, dizziness, anorexia, fatigue, edema, skin rash, leg pain, inguinal adenopathy, medication taste, and sore throat.

**Long-Term Administration:** The most frequent adverse events reported in a clinical trial for the

prevention of recurrences with continuous administration of 400 mg (two 200 mg capsules) 2 times daily for 1 year in 586 patients treated with Acyclovir were: nausea (4.8%), diarrhea (2.4%), headache (1.9%) and rash (1.7%). The 589 control patients receiving intermittent treatment of recurrences with Acyclovir for 1 year reported diarrhea (2.7%), nausea (2.4%), headache (2.2%) and rash (1.5%).

The most frequent adverse events reported during the second year by 390 patients who elected to continue daily administration of 400 mg (two 200 mg capsules) 2 times daily for 2 years were headache (1.5%), rash (1.3%) and paresthesia (0.8%). Adverse events reported by 329 patients during the third year included asthenia (1.2%), paresthesia (1.2%) and headache (0.9%).

**Herpes Zoster:** The most frequent adverse events reported during three clinical trials of treatment of herpes zoster (shingles) with 800 mg of oral Acyclovir 5 times daily for 7 to 10 days in 323 patients were: malaise (11.5%), nausea (8.0%), headache (5.9%), vomiting (2.5%), diarrhea (1.5%) and constipation (0.9%). The 323 placebo recipients reported malaise (11.1%), nausea (11.5%), headache (11.1%), vomiting (2.5%), diarrhea (0.3%) and constipation (2.4%).

**Chickenpox:** The most frequent adverse events reported during three clinical trials of treatment of chickenpox with oral Acyclovir in 495 patients were: diarrhea (3.2%), abdominal pain (0.6%), rash (0.6%), vomiting (0.6%) and flatulence (0.4%). The 498 patients receiving placebo reported: diarrhea (2.2%), flatulence (0.8%) and insomnia (0.4%).

**Observed During Clinical Practice:** Based on clinical practice experience in patients treated with oral Acyclovir in the U.S., spontaneously reported adverse events are uncommon. Data are insufficient to support an estimate of their incidence or to establish causation. These events may also occur as part of the underlying disease process. Voluntary reports of adverse events which have been received since market introduction include:

**General:** fever, headache, pain, peripheral edema, and rarely, anaphylaxis

**Nervous:** confusion, dizziness, hallucinations, paresthesia, somnolence (These symptoms may be marked, particularly in older adults.)

**Digestive:** diarrhea, elevated liver function tests, gastrointestinal distress, nausea

**Hemic and Lymphatic:** leukopenia, lymphadenopathy

**Musculoskeletal:** myalgia

**Skin:** alopecia, pruritus, rash, vesicles → urticaria

**Special Senses:** visual abnormalities

**Urogenital:** elevated creatinine

**OVERDOSAGE:** Patients have ingested intentional overdoses of up to 100 capsules (20 g) of Acyclovir, with no unexpected adverse effects.

Precipitation of acyclovir in renal tubules may occur when the solubility (2.5 mg/mL) in the intratubular fluid is exceeded. Renal lesions considered to be related to obstruction of renal tubules by precipitated drug crystals occurred in the following species: rats treated with i.v. and i.p. doses of 20 mg/kg/day for 21 and 31 days, respectively, and at s.c. doses of 100 mg/kg/day for 10 days;

peritoneal  
 rabbits at s.c. and i.v. doses of 50 mg/kg/day for 13 days; and dogs at i.v. doses of 100 mg/kg/day for 31 days. A 6-hour hemodialysis results in a 60% decrease in plasma acyclovir concentration. Data concerning peritoneal dialysis are incomplete but indicate that this method may be significantly less efficient in removing acyclovir from the blood. In the event of acute renal failure and anuria the patient may benefit from hemodialysis until renal function is restored (see DOSAGE AND ADMINISTRATION).

#### DOSAGE AND ADMINISTRATION:

**Treatment of Initial Genital Herpes:** 200 mg (one 200 mg capsule) every 4 hours, 5 times daily for 10 days.

For  
**Chronic Suppressive Therapy for Recurrent Disease:** 400 mg (two 200 mg capsules or one 400 mg tablet) 2 times daily for up to 12 months, followed by re-evaluation. See INDICATIONS AND USAGE and PRECAUTIONS for considerations on continuation of suppressive therapy beyond 12 months. Alternative regimens have included doses ranging from 200 mg 3 times daily to 200 mg 5 times daily.

**Intermittent Therapy:** 200 mg (one 200 mg capsule) every 4 hours, 5 times daily for 5 days. Therapy should be initiated at the earliest sign or symptom (prodrome) of recurrence.

**Acute Treatment of Herpes Zoster:** 800 mg (four 200 mg capsules, two 400 mg tablets or one 800 mg tablet) every 4 hours orally, 5 times daily for 7 to 10 days.

**Treatment of Chickenpox: Children (2 years of age and older):** 20 mg/kg per dose orally four times daily (80 mg/kg/day) for 5 days. Children over 40 kg should receive the adult dose for chickenpox.

**Adults and Children over 40 kg:** 800 mg four times daily for 5 days.

Therapy should be initiated at the earliest sign or symptom of chickenpox to derive the maximal benefits of therapy.

**Patients With Acute or Chronic Renal Impairment:** Comprehensive pharmacokinetic studies have been completed following intravenous acyclovir infusions in patients with renal impairment. Based on these studies, dosage adjustments are recommended in the following chart for genital herpes and herpes zoster indications:

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER        74976

CORRESPONDENCE



GENPHARM

January 6, 1998

Office of Generic Drugs, CDER, FDA  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room 150  
Rockville, Maryland 20855

RE: **ANDA No. 74-977**  
**ACYCLOVIR CAPSULES**  
**200 mg**

NDA ORIG AMENDMENT

N/E

1/4/98  
FA noted.  
① To Chemistry Reviewer  
② To Labeling Reviewer.  
FACSIMILE AMENDMENT  
FPL  
ins...  
S...  
...  
21-110

Dear Sirs/Madam:

Please find enclosed our **FACSIMILE AMENDMENT** to ANDA # 74-977 in response to the faxed letter dated Dec. 9, 1997 from Timothy Ames, Project Manager for this ANDA.

For the reviewers' convenience, we have:

- a) attached a copy of the letter dated Dec. 9, 1997;
- b) formatted our amendment such that each comment made by the reviewer has been restated in **bold print** and is followed by our response.

We have enclosed one (1) archival, one (1) review, and one (1) field copy of the application in accordance with 21 CFR § 314.55. We certify that the Field Copy is a true copy of the technical section contained in the archival and review copies of this application and has been submitted to the Office of Generic Drugs.

We trust the information submitted is sufficient for this amendment to be evaluated. If there are any questions with respect to this application, you may direct written and telephoned communications to Ms. Anita M. Goodman at (212) 223-1282 or you may contact Genpharm directly at 1-800-661-7134.

Thank you for your prompt handling of this submission.

Yours Sincerely,  
Genpharm Inc.

Richard K. Pike  
Director, Regulatory Affairs

**RECEIVED**  
JAN 08 1998  
**GENERIC DRUGS**  
Date 6<sup>th</sup> January '98

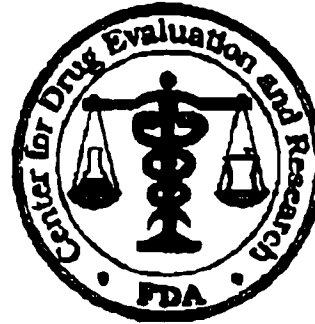


**FACSIMILE AMENDMENT**

DEC 9 1997

ANDA 74-977

OFFICE OF GENERIC DRUGS, CDER, FDA  
 Document Control Room, Metro Park North II  
 7500 Standish Place, Room 150  
 Rockville, MD 20855-2773 (301-594-0320)



TO: APPLICANT: Genpharm Inc. PHONE: 212-223-1282  
 ATTN: Anita Goodman, M.D. (US Agent) FAX: 212-223-1398

FROM: Timothy Ames PROJECT MANAGER (301) 827-5849

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated September 27, 1996, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Acyclovir Capsules 200mg.

Reference is also made to your amendment(s) dated October 1, 1997.

Attached are \_\_\_ pages of minor deficiencies and/or comments that should be responded to within 30 calendar days from the date of this document. This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed. Your complete response should be (1) faxed directly to our document control room at 301- 827-4337, (2) mailed directly to the above address, and (3) the cover sheet should be clearly marked a FACSIMILE AMENDMENT.

Please note that if you are unable to provide a complete response within 30 calendar days, the file on this application will be closed as a MINOR AMENDMENT and you will be required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Accordingly, a response of greater than 30 days should be clearly marked MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. Facsimiles or incomplete responses received after 30 calendar days will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data.

**SPECIAL INSTRUCTIONS:**

**THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.** If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

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DEC 9 1997

**38. Chemistry Comments to be Provided to the Applicant**ANDA: 74-977 APPLICANT: Genpharm Inc.DRUG PRODUCT: Acyclovir Capsules, 200 mg

The deficiencies presented below represent FACSIMILE deficiencies.

**A. Deficiencies****1. Regarding Laboratory Controls (Finished Dosage Form):**

Please revise and resubmit your finished product specifications and Certificate of Analysis (COA) and change your Dissolution specification to NLT (Q) in 30 minutes (refer to the Division of Bioequivalence letter dated October 9, 1997).

**2. Regarding Stability:**

Please revise and resubmit your stability specifications and stability reports and change your Dissolution specification to NLT (Q) in 30 minutes (refer to the Division of Bioequivalence letter dated October 9, 1997).

Sincerely yours,

*fr* Frank O. Holcombe, Jr., Ph.D.  
Director  
Division of Chemistry II  
Office of Generic Drugs  
Center for Drug Evaluation and Research



GENPHARM

**Telephone Amendment**

Office of Generic Drugs, CDER, FDA  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room 150  
Rockville, Maryland 20855

NEW YORK  
NC

**RE: ANDA No. 74-977  
ACYCLOVIR CAPSULES  
200 mg**

FEB 20 1998

Dear Sirs/Madam:

Please find enclosed a Telephone Amendment to ANDA# 74-977.

For the reviewer's convenience, we have:

- a) formatted our amendment such that each comment made by the reviewer has been restated in *italic* print;
- b) provided our response following the comment.

We have enclosed one (1) archival, one (1) review copy and one (1) field copy of the application in accordance with 21 CFR § 314.55. In each copy, a signed form FDA 356h by our US agent is submitted. We certify that the Field Copy is a true copy of the technical section contained in the archival and review copies of this application and has been submitted to the Office of Generic Drugs.

We trust the information submitted is sufficient for this amendment to be evaluated. If there are any questions with respect to this application, you may direct written and telephone communications to Genpharm at 1-800-661-7134 or you may contact our U.S. agent, Dr. Anita M. Goodman of Lipha Pharmaceuticals, Inc. New York, New York, at (212) 223-1282.

Thank you for your prompt handling of this submission.

Yours Sincerely,  
**Genpharm Inc.**

Richard K. Pike  
Director, Regulatory Affairs

RECEIVED  
FEB 25 1998  
GENERIC DRUGS





**GENPHARM**

Office of Generic Drugs, CDER, FDA  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room 150  
Rockville, Maryland 20855

AM noted  
① To Chemistry Division  
② To Labeling Division  
for review  
10/1/97

✓ **MINOR  
AMENDMENT**

**RE: ANDA No. 74-977  
ACYCLOVIR CAPSULES  
200 mg**

7PL  
NOA ORIG AMENDMENT  
1.1

OCT 01 1997

Dear Sirs/Madam:

Please find enclosed a **MINOR AMENDMENT** to ANDA # 74-977 in response to the faxed letter dated May 14, 1997 from Tim Ames, Project Manager which we received on May 23, 1997.

For the reviewers' convenience, we have:

- a) attached a copy of the letter dated May 14, 1997;
- b) formatted our amendment such that each comment made by the reviewer has been restated in *italic* print;
- c) provided our response following the comment.

We have enclosed one (1) archival and one (1) review copy of the application in accordance with 21 CFR § 314.55. We also hereby certify that the Field Copy is a true copy of the technical section contained in the archival and review copies of this application and has been submitted to the Office of Generic Drugs.

We trust the information submitted is sufficient for this amendment to be evaluated.

Along with our responses, a signed form FDA 356h by our US agent, Dr. Anita Goodman of Lipha Pharmaceuticals, Inc., New York, N.Y. is submitted. Although Dr. Anita Goodman is our US Agent, should you have any questions, please contact the undersigned at 1-800-661-7134.

Thank you for your prompt handling of this submission.

Yours Sincerely,  
**Genpharm Inc.**

Richard K. Pike  
Director, Regulatory Affairs

**RECEIVED**

OCT 03 1997

**GENERIC DRUGS**

Madison



MINOR AMENDMENT

MAY 14 1997

ANDA/~~74-977~~ 74-977



OFFICE OF GENERIC DRUGS, CDER, FDA  
Document Control Room, Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

TO: APPLICANT Genpharm Inc. PHONE 212-223-1272  
ATTN: Dr. Anita M. Goodman FAX 212-223-1398

FROM: Tim A... PROJECT MANAGER (301-~~884~~  
827-5849)

Dear Sir/Madam: Dr. Goodman

This facsimile is in reference to your abbreviated new drug/ antibiotic application dated 9/27/97, submitted pursuant to Section 505(j)/507 of the Federal Food, Drug, and Cosmetic Act for Amoxicillin Capsules, 200mg

Reference is also made to your amendment(s) dated       

The application is deficient and, therefore not approvable under Section 505/507 of the Act for the reasons provided in the attachments (11 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing. For further clarification or assistance please contact the Project Manager listed above.

SPECIAL INSTRUCTIONS: Please refer to the letter dated 4/30/97 from the Division of Bioequivalence. The response to this Fax should not be submitted until you respond to the 4/30/97 letter.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

x:\newlog\admin\fdcrak\faxcov.mss

MAY 14 1991

38. Chemistry Comments to be Provided to the Applicant

ANDA: 74-977 APPLICANT: Ganpharm Inc.

DRUG PRODUCT: Acyclovir Capsules, 200 mg

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

ANDA 74-977

5. Regarding Stability:

- a. Please revise and resubmit your stability reports to include the formulation and manufacturer of the active ingredient. This information may be attached to the stability report.
- b. Please revise and resubmit your stability reports to include

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

Please be advised that the suitability of the proposed dissolution procedure and specification will be established upon completion of review by the Division of Bioequivalence.

Sincerely yours,

/ s /

Lr

---

Frank O. Holcombe, Jr., Ph.D.  
 Director  
 Division of Chemistry II  
 Office of Generic Drugs  
 Center for Drug Evaluation and Research



GENPHARM

*Telephone Amendment*

Office of Generic Drugs, CDER, FDA  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room 150  
Rockville, Maryland 20855

SEP 08 1997

**RE: ACYCLOVIR CAPSULES 200 mg ANDA (ANDA No. 74-977)  
Comparative Dissolution Profiles**

Dear Sirs:

As discussed in a telephone request with Ms. Lizzie Sanchez on September 4, 1997, to assist the reviewer, we have enclosed all the comparative dissolution profiles for the above mentioned ANDA. The comparative dissolution profiles will consist of the individual dissolution data, statistical summary, and a dissolution study cover page specifying the dissolution parameters used.

Please note, the first comparative dissolution testing was performed with Genpharm's in house method SP0049.A. (dissolution medium 0.1N HCl, which will be the medium specified in the upcoming Pharmacopeial Forum (see letter attached). FDA had later requested for comparative dissolution to be performed in water as per the Pharmacopeial Forum (volume 22, number 4, page 2487).

Accompanied in this amendment is a form FDA 356h signed by our US agent, Dr. Anita Goodman of Lipha Pharmaceuticals, Inc., New York, N.Y. The pages of the dissolution data have been paginated on the bottom right hand corner of the page.

An archival copy and the review copy is provided.

...cont'd

RECEIVED

SEP 10 1997

GENERIC DRUGS



Should you have any questions, please contact the undersigned at 1-800-661-7134.

Thank you for your prompt handling of this submission.

Yours Sincerely,  
**Genpharm Inc.**

A handwritten signature in black ink, appearing to read "R. K. Pike". The signature is fluid and cursive, with a large initial "R" and a long horizontal stroke extending to the right.

Richard K. Pike  
Director, Regulatory Affairs





GENPHARM

Office of Generic Drugs, CDER, FDA  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room 150  
Rockville, Maryland 20855

NAI  
"Bio Assigned"  
[Signature]  
7/3/97

**FACSIMILE  
AMENDMENT**

NEW CORRESP BIOAVAILABILITY

12/80

RE: ANDA No. 74-977  
ACYCLOVIR CAPSULES  
200 mg ANDA

JUN 02 1997

Dear Sirs/Madam:

Please find enclosed a **FACSIMILE AMENDMENT** to ANDA # 74-977 in response to the faxed letter dated Apr. 30, 1997 from Lizzie Sanchez, Project Manager which we received on May 2, 1997.

For the reviewers' convenience, we have:

- a) attached a copy of the letter dated Apr. 30, 1997;
- b) formatted our amendment such that each comment made by the reviewer has been restated in *italic* print;
- c) provided our response following the comment.

We have enclosed one (1) archival and one (1) review copy of the application in accordance with 21 CFR § 314.55.

We trust the information submitted is sufficient for this amendment to be evaluated. Dr. Anita Goodman is our US Agent, however, should you have any questions, please contact the undersigned at 1-800-661-7134.

Along with our responses, a signed form FDA 356h by our US agent, Dr. Anita Goodman of Lipha Pharmaceuticals, Inc., New York, N.Y. is submitted.

Thank you for your prompt handling of this submission.

Yours Sincerely,  
**Genpharm Inc.**

[Signature]  
for Richard K. Pike  
Director, Regulatory Affairs

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JUN 04 1997

GENERIC DRUGS

[Handwritten signature]  
6-20-97





GENPHARM

Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food & Drug Administration  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

NEW CORRESP

*Noted*

*Note  
- 11/11/97  
5/14/97*

ACKNOWLEDGEMENT

*11/11/97  
MPC*

Re: Acyclovir Capsules 200 mg (ANDA # 74-977)

We acknowledge receipt of your letter dated Apr. 30, 1997 from Dr. Nicholas Fleischer of the Division of Bioequivalence, which we received on May 5, 1997.

We are currently addressing the comments made by the reviewer and will file an amendment when the response is complete.

If there are any questions with respect to this application, you may direct written and telephoned communications to Genpharm at 1-800-661-7134 or you may contact our U.S. agent, Ms. Anita M. Goodman, at (212) 223-1282.

Yours sincerely

*R. K. Pike*

Richard Pike  
Director, Regulatory Affairs  
GENPHARM INC.

*9<sup>th</sup> May 97*  
(date)

cc: Ms. Anita M. Goodman, M.D.  
Executive Vice President & Chief Operating Officer  
Lipha Pharmaceuticals, Inc.  
9 West 57th St., Suite 3825  
New York, NY 10019-2701

RECEIVED

MAY 12 1997

GENERIC DRUGS

*Anita M. Goodman  
5/14/97*



2.1  
C-12345 N1

ANDA 74-977

APR 30 1997

Lipha Pharmaceuticals, Inc.  
U.S. Agent for Genpharm, Inc.  
Attention: Anita M. Goodman  
9 West 57th Street, Suite 3825  
New York NY 10019-2701

|||||.....|||||.....|||||.....

Dear Madam:

Reference is made to the Abbreviated New Drug Application submitted on September 27, 1996 and amendments dated January 16, 22 and February 5, 1997, for Acyclovir Capsules, 200 mg.

The Office of Generic Drugs has reviewed the bioequivalence data submitted and the following comments are provided for your consideration:

1. The following subjects in the fasting study exhibited an increase in the terminal phase of their plasma concentration time curves:

Treatment-Test

| Subject | Time | Conc |
|---------|------|------|
|---------|------|------|

Treatment-Reference

| Subject | Time | Conc |
|---------|------|------|
|---------|------|------|

Please explain how these subjects were determined to be in the log-linear phase, since the terminal data was increasing.

2. The data for the subjects in deficiency 1 should be deleted from the estimation of  $AUC(0-\infty)$ .
3. Explain why the reported value in the long-term stability study for \_\_\_\_\_ different from the standard.
4. The lot of drug used in the bio-study was 102666, which seemed to be prepared from bulk lot 102130. However, the dissolution data for the test was collected on lot 102707. Is lot 102707 the same or different from the bio-lot? If it is not the same lot the dissolution study must be repeated using the appropriate lot.

As described under 21 CFR 314.96, an action which will amend this application is required, should you have any questions, please call Lizzie Sanchez, Pharm.D., Project Manager, at (301) 594-2290. In future correspondence regarding this issue, please include a copy of this letter.

Sincerely yours,

^

*fw*

Nicholas Fleischer, Ph.D.  
Director  
Division of Bioequivalence  
Office of Generic Drugs  
Center for Drug Evaluation and Research



GENPHARM

BIOAVAILABILITY  
BIO  
NEW  
NC/B

January 16, 1997

Office of Generic Drugs, CDER, FDA  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room E150  
Rockville, Maryland 20855-2773

Bill J...  
MAY 1997

**Attention:** Mr. Larry Galvin  
cc: Ms. Lizzie Sanches

**REF:** ANDA 74-977  
Acyclovir Capsules 200 mg

**Re:** Bioequivalence Data Diskettes

Further to a call from Mr. Larry Galvin we have included diskettes (total 2 diskettes) containing the Biostudy data for 200 mg Acyclovir capsules. One diskette contains the data for the project no 1645, and the other diskette contains the data for the project no 1643.

Also attached are the hard copies of File Information.

Two copies of the information is being submitted - Review Copy (Orange Folder), and Archival Copy (Blue Folder). The diskettes are included only in the Orange Folder.

We trust the information provided is satisfactory for your review. Should you have any questions or require further clarification please do not hesitate to contact us.

Sincerely,  
Genpharm Inc.

Richard K. Pike  
Director, Regulatory Affairs

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JAN 17 1997

GENERIC





GENPHARM

January 22, 1997

Office of Generic Drugs, CDER, FDA  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room 150  
Rockville, Maryland 20855

*Bill Juto  
NRE 12/2/97*

RE: Dissolution Data for ACYCLOVIR CAPSULES 200 mg ANDA  
(ANDA No. 74-977)

Dear Sirs:

Please find enclosed dissolution data as requested by Lizzie Sanchez in a telephone conversation on January 21, 1997 for the above mentioned ANDA.

This submission consist of 1 volume containing the dissolution data, accompanied by a form FDA 356h signed by our US agent, Dr. Anita Goodman of Lipha Pharmaceuticals, Inc., New York, N.Y. The dissolution data are provided in their respective section of the ANDA for placement into the original ANDA.

Two copies of volume 1 are submitted, an archival copy (blue folder) and the review copy (orange folder).

Should you have any questions, please contact the undersigned at 1-800-661-7134.

Thank you for your prompt handling of this submission.

Yours Sincerely,  
**Genpharm Inc.**

*R. K. Pike*

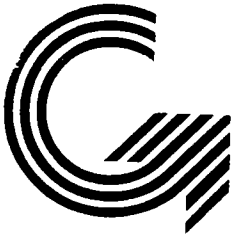
Richard K. Pike  
Director, Regulatory Affairs

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JAN 27 1997

GENERIC DRUGS





GENPHARM

February 5, 1997

Office of Generic Drugs, CDER, FDA  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room 150  
Rockville, Maryland 20855

*Bill Smith  
2/5/97*

GEN PHARM

**RE: ACYCLOVIR CAPSULES 200 mg (ANDA No. 74-977)  
Comparative Dissolution Profiles using PF volume 22, Number 4 dissolution method  
(p.2487)**

Dear Sirs:

Please find enclosed comparative dissolution profile with the individual dissolution data using PF volume 22, Number 4 dissolution method as requested by Lizzie Sanchez in a telephone conversation on January 24, 1997 for the above mentioned ANDA.

This submission consist of 1 volume containing the dissolution data, accompanied by a form FDA 356h signed by our US agent, Dr. Anita Goodman of Lipha Pharmaceuticals, Inc., New York, N.Y. The dissolution data are provided in their respective section of the ANDA for placement into the original ANDA.

Two copies of volume 1 are submitted, an archival copy (blue folder) and the review copy (orange folder).

Should you have any questions, please contact the undersigned at 1-800-661-7134.

Thank you for your prompt handling of this submission.

Yours Sincerely,  
Genpharm Inc.

Richard K. Pike  
Director, Regulatory Affairs

RECEIVED

FEB 07 1997

GENERIC DRUGS



ANDA 74-977

Lipha Pharmaceuticals Inc.  
Attention: Anita M. Goodman, M.D.  
U.S. Agent for: Genpharm Inc.  
9 West 57th Street  
Suite 3825  
New York, NY 10019-2701

DEC 3 1996

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Acyclovir Capsules 200 mg

DATE OF APPLICATION: September 27, 1996

DATE OF RECEIPT: October 10, 1996

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

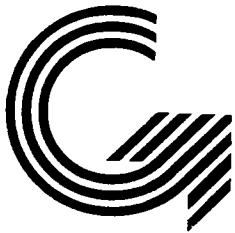
Tim Ames  
Project Manager  
(301) 594-0305

Sincerely yours,

12/3/96

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





GENPHARM

September 27, 1996

Office of Generic Drugs  
CDER, Food & Drug Administration  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room 150  
Rockville, Maryland 20855-2773

RECEIVED

OCT 10 1996

GENERIC DRUGS

**RE:**

ANDA for 200 mg Capsules

Dear Director, Office of Generic Drugs:

Genpharm Inc. submits today an original abbreviated new drug application ("ANDA") seeking approval to market a 200 mg Acyclovir capsule that is bioequivalent to the listed drug, Zovirax® (Acyclovir), manufactured by Glaxo Wellcome Inc. pursuant to NDA #18828 001.

This ANDA consists of six volumes. Genpharm is filing an archival copy (in blue folders) of the ANDA that contains all the information required in the ANDA and a technical review copy (in red folders) which contains all the information in the archival copy with the exception of the Bioequivalence section (VI). A separate copy of the Bioequivalence section is provided in the orange folder.

For more detailed information of the organisation of the ANDA, please refer to the introduction page, "Executive Summary - Organisation of the ANDA."

A letter from Genpharm Inc. appointing Anita Goodman as the Agent in the United States immediately follows the Executive Summary.

This also certifies that, concurrently with the filing of this ANDA, a true copy of the technical sections of the ANDA (including a copy of the 356h form and a certification that the contents are a true copy of those filed with the Office of Generic Drugs) was sent to our local district office. This "field copy" was contained in a burgundy folder.

We request that all information in this file be treated as confidential within the meaning of 21 CFR section 314.430 and that no information from the file be submitted to an applicant without our



written consent to an authorized member of your Office.

Should you have any questions regarding the information in this submission, please ~~not~~ not hesitate to call me at 1-800-661-7134.

Thank you for your prompt handling of this submission.

Sincerely,  
**Genpharm Inc.**

A handwritten signature in cursive script that reads "Richard K. Pike". The signature is written in dark ink and is positioned above the typed name.

Richard K. Pike  
Director, Regulatory Affairs

RECORD OF TELEPHONE CONVERSATION

DATE: 2/9/98

PRODUCT NAME: Acyclovir Tablets, 400 mg & 800 mg  
Acyclovir Capsules, 200 mg

ANDA/AADA NUMBER: 74-976 & 74-977

MANUFACTURER NAME: Genpharm Inc.

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD:  
Bruce Goddard  
Alpha Pharmaceuticals, U.S. Agent  
Reg. Affairs  
(2) 223-1280

PARTICIPANT(S) TELEPHONE:  
Norman R. Gregory, Review Chemist, Branch VI , OGD, CDER, FDA

MINUTES OF CONVERSATION:  
called the U.S. agent do they could convey the following concerns to the applicant:

These concerns will be conveyed to the applicant and their response faxed followed by hard copy.

NAME OF OGD REPRESENTATIVE: Norman R. Gregory

SIGNATURE OF OGD REPRESENTATIVE:

DIVISION/BRANCH: Office of Generic Drugs  
Division II, Branch VI.

MINUTES PREPARED BY:

Mr. Norman R. Gregory, Review Chemist, Branch VI , OGD, CDER, FDA



GENPHARM

January 22, 1997

*Bio. Info.  
MRE 12/2/97*

Office of Generic Drugs, CDER, FDA  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room 150  
Rockville, Maryland 20855

**RE: Dissolution Data for ACYCLOVIR CAPSULES 200 mg ANDA  
(ANDA No. 74-977)**

Dear Sirs:

Please find enclosed dissolution data as requested by Lizzie Sanchez in a telephone conversation on January 21, 1997 for the above mentioned ANDA.

This submission consist of 1 volume containing the dissolution data, accompanied by a form FDA 356h signed by our US agent, Dr. Anita Goodman of Lipha Pharmaceuticals, Inc., New York, N.Y. The dissolution data are provided in their respective section of the ANDA for placement into the original ANDA.

Two copies of volume 1 are submitted. an archival copy (blue folder) and the review copy (orange folder).

Should you have any questions, please contact the undersigned at 1-800-661-7134.

Thank you for your prompt handling of this submission.

Yours Sincerely,  
**Genpharm Inc.**

Richard K. Pike  
Director, Regulatory Affairs

**RECEIVED**

**JAN 27 1997**

**GENERIC DRUGS**



RECORD OF TELEPHONE CONVERSATION

DATE: 2/12/98

PRODUCT NAME: Acyclovir Tablets, 400 mg & 800 mg  
Acyclovir Capsules, 200 mg

FDA/AADA NUMBER: 74-776 & 74-977

FIRM NAME: Genpharm Inc.

NAME AND TITLE OF PERSON WITH  
WHOM CONVERSATION WAS HELD:  
Jim Chu, Regulatory Affaires Associate  
(800) 661-7134

PARTICIPANT(S) TELEPHONE:  
Mr. Norman R. Gregory, Review Chemist, Branch VI , OGD, CDER, FDA

MINUTES OF CONVERSATION:  
Returned firms phone call to clarify questions from phone memo of  
2/9/98 regarding the following:

This information will be submitted.

NAME OF OGD REPRESENTATIVE: Norman R. Gregory

SIGNATURE OF OGD REPRESENTATIVE:

DIVISION/BRANCH: Office of Generic Drugs  
Division II, Branch VI.

MINUTES PREPARED BY:

Mr. Norman R. Gregory, Review Chemist, Branch VI , OGD, CDER, FDA



GENPHARM

BIOAVAILABILITY  
BIOSTUDY  
NEW ORIGIN

NC/B

January 16, 1997

Office of Generic Drugs, CDER, FDA  
Document Control Room  
Metro Park North II,  
7500 Standish Place, Room E150  
Rockville, Maryland 20855-2773

Bio. Info.  
MAI 10/24/97

**Attention:** Mr. Larry Galvin  
**cc:** Ms. Lizzie Sanches

**REF:** ANDA 74-977  
Acyclovir Capsules 200 mg

**Re:** Bioequivalence Data Diskettes

Further to a call from Mr. Larry Galvin we have included diskettes (total 2 diskettes) containing the Biostudy data for 200 mg Acyclovir capsules. One diskette contains the data for the project no 1645, and the other diskette contains the data for the project no 1643.

Also attached are the hard copies of File Information.

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We trust the information provided is satisfactory for your review. Should you have any questions or require further clarification please do not hesitate to contact us.

Sincerely,  
Genpharm Inc.

Richard K. Pike  
Director, Regulatory Affairs

RECEIVED

JAN 17 1997

GENERIC DRUGS

