CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75211

CORRESPONDENCE

ANDA 75-211

Mylan Pharmaceuticals Inc.
Attention: Frank R. Sisto
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504-4310

OCT 22 1997

Dear Sir:

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 Tablets, 400 mg and 800 mg

DATE OF APPLICATION: September 29, 1997

DATE OF RECEIPT: September 30, 1997

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) 827-5848

Sincerely yours,

/S/

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

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

NEW CORRESP

BIOAVAILABILITY
NDA #20

NAI [illegible] 7/10/98

JUL 8 1998

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

BIOEQUIVALENCE AMENDMENT

RE: ACYCLOVIR TABLETS, 400MG AND 800MG
ANDA #75-211
RESPONSE TO AGENCY CORRESPONDENCE DATED JUNE 10, 1998

Dear Mr. Sporn:

Reference is made to the ANDA identified above, which is currently under review, and to the comments from the Division of Bioequivalence which were forwarded to Mylan by facsimile in correspondence from the Office of Generic Drugs dated June 10, 1998. In response to the bioequivalence comments in the June 10 correspondence, Mylan wishes to amend the application as follows:

A. REGARDING BIOEQUIVALENCE ISSUES:

FDA COMMENT 1. The Division of Bioequivalence has completed its review and has no further questions at this time.

Please acknowledge that the following dissolution testing specifications have been incorporated into your stability and quality control programs:

> The dissolution testing should be conducted in 900mL of water, at 37°C using USP Apparatus 2 (Paddle) at 50rpm. The test product should meet the following specifications:
>
> Not less than % (Q) of the labeled amount of the drug in the dosage form is dissolved in 45 minutes.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

RECEIVED
JUL 09 1998
GENERIC DRUGS

Department—Fax Numbers		Information Systems	(304) 285-6404	Pr[illegible]	[illegible]98-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Q[illegible]	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

MYLAN RESPONSE: The dissolution testing requested by the Division of Bioequivalence has already been incorporated into Mylan's stability and quality control programs. This testing is identical to that which was previously proposed in the original ANDA for the above referenced product which was submitted on September 29, 1997 (Volume 1.8, Section XV).

It is also acknowledged and understood that the bioequivalency comments expressed in the letter dated June 10, 1998 are preliminary and may be revised after review of the entire application.

For your reference, a copy of the Agency correspondence dated June 10, 1998 is enclosed.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/tlr

enclosures

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

FYI

NDA ORIG AMENDMENT

N/FA

JUL 8 1998

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JUL 09 1998

GENERIC DRUGS

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn, Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

FACSIMILE AMENDMENT

RE: ACYCLOVIR TABLETS, 400MG AND 800MG
ANDA #75-211
RESPONSE TO AGENCY CORRESPONDENCE DATED JUNE 10, 1998

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to the comments from the Agency regarding this application which were provided to Mylan in a facsimile dated June 10, 1998. In response to the Agency's June 10, 1998 comments, Mylan wishes to amend this application as follows.

A. REGARDING CHEMISTRY ISSUES

FDA COMMENT 1. We note that the differences between Exhibit and Production size batch records were provided for the specifications of tolerance listed in the final blend and the tablet yield for each strength. We also note that the differences between 400mg product and 800mg product were provided for the specifications of tolerance listed in the final blend and the tablet yield. Please provide justification.

MYLAN RESPONSE: The justification for the difference between the final blend specification of tolerances and the tablet yield specification of tolerances for the Exhibit versus the Production size batch records and for the 400mg versus the 800mg tablet strengths is the blender size used to produce each batch. The specification of tolerances at Mylan is determined through information relating to blender size used for processing; the greater the capacity, the more narrow the tolerance. First, the Production size batch record produces a larger tablet yield than an Exhibit size batch record tablet yield (, thus requiring a larger blender size and a tighter specification of tolerance. Secondly, the 800mg product has a larger ingredient batch quantity than the 400mg product (1260.0kg vs. 630kg) This amount requires a larger blender capacity(125 cu. ft. "V" blender vs. 50 cu. ft. "V" blender) and thus a tighter specification of tolerance for each production process (i.e. final blend).

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

FDA COMMENT 2. We note that the assay limits for granulation intermediate is given as % . The in-process specification for Acyclovir should be tighter than the release specification. Please revise.

MYLAN RESPONSE: Acyclovir, USP contains up to % water, and no adjustment for this water is made in the manufacturing directions for Acyclovir Granulation Intermediate. The assay limits of % for Acyclovir Granulation Intermediate is a release specification, not an in-process specification, and was established to take into account the initial water content of the drug, the % Povidone present in the intermediate, as well as potential processing losses incurred during the manufacture of the granulation intermediate. Acyclovir tablets, 400 mg and 800 mg have a release specification of % which was established to take into account typical processing losses and variability normally encountered during blending, tableting, and coating. Since Acyclovir Granulation Intermediate and Acyclovir Tablets are manufactured and released under separate batch tickets, each of these final products has an appropriate, independent release specification.

FDA COMMENT 3. Submit the actual torque test for cap removal covering the 100's and 500's Tablets package sizes for each strength.

MYLAN RESPONSE: In accordance with Mylan SOP-4012, the specifications for torques (in-lbs)for lids from the capper are to be a target/average of 8 with an individual lower range of 6 and an individual upper range of 21. The following table describes the torque testing results covering the 100's and 500's Tablets package sizes for each strength of Acyclovir Tablets.

STRENGTH	BOTTLE SIZE	RESULT (IN-LBS)
400MG (2C004L)	100 TABLETS	AVG. = 13
400MG (2C004L)	500 TABLETS	AVG. = 14
800 MG (2C005L)	100 TABLETS	AVG. = 14
800 MG (2C005L)	500 TABLETS	AVG. = 14

B. REGARDING MISCELLANEOUS ISSUES

FDA COMMENT 1. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

Your methods for drug product have been submitted for validation by the FDA labs. Please send samples of drug substance, drug product, Guanine and other standards when requested by the district lab.

MYLAN RESPONSE: Mylan acknowledges that our methods for the drug product have been submitted for validation by the FDA labs. Mylan forwarded samples of drug substance, drug product (400 mg), Guanine, and other standards on May 13, 1998, as requested by the Baltimore District Lab.

C. REGARDING LABELING ISSUES

MYLAN RESPONSE: Attachment C contains twelve (12) copies of the following final printed bottle labels and package outserts for Acyclovir Tablets, 400 mg and 800 mg.

BOTTLE LABELS

400 mg	100 tablets	Code - RM0253A
	500 tablets	Code - RM0253B
800 mg	100 tablets	Code - RM0302A
	500 tablets	Code - RM0302B

PACKAGE OUTSERT
Code - **ACYCT:R1**; REVISED JUNE 1998

The enclosed labeling incorporates the revisions requested in the Agency's letter dated June 10, 1998. A copy of this letter is provided in Attachment A for the convenience of the reviewer.

In order to facilitate the review of this labeling and in accordance with 21 CFR 314.94(a)(8)(iv), Attachment B contains a side-by-side comparison of the final printed labeling to the labeling that was previously submitted. It is noted that prior to approval of this application the agency reserves the right to request further changes in the Mylan labeling based upon the changes in the approved labeling of the listed drug or upon further review of the application.

A copy of the Agency correspondence dated June 10, 1998 is included in Attachment A, for the convenience of the reviewer.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of the technical sections of this amendment, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore District Office.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned by phone at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/tlr

enclosures

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

SEP 29 1997

ELECTRONIC DATA ENCLOSED
BIOEQUIVALENCE DATA ENCLOSED

505(j)(11) a OK
10/14/97
Gregory S. Levin

Office of Generic Drugs, CDER, FDA
Douglas L. Sporn Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: ACYCLOVIR TABLETS, 400 MG AND 800 MG

Dear Mr. Sporn:

Pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act and 21 CFR § 314.92 and 314.94, we submit the enclosed abbreviated new drug application for:

Proprietary Name: None
Established Name: Acyclovir Tablets
This application consists of a total of 17 volumes.
- Archival Copy - 8 volumes.
- Review Copy - 9 volumes.
  - Technical Section For Chemistry - 3 volumes.
  - Technical Section For Pharmacokinetics - 6 volumes.
- Analytical Methods - 2 extra copies; 1 volume each.

NOTE: The Technical Section for Pharmacokinetics of the review copy and the archival copy each contain a data diskette for the bioequivalence study conducted in support of this application.

This application provides for the manufacture of Acyclovir Tablets, 400 mg and 800 mg. All operations in the manufacture, packaging, and labeling of the drug product are performed by Mylan Pharmaceuticals Inc., 781 Chestnut Ridge Road, Morgantown, WV 26505-2730.

As required by 21 CFR 314.94(d)(5) we certify that a true copy of the technical sections of this application, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore District Office. The following Table of Contents and Reader's Guide detail the documentation submitted in support of this application.

All correspondence regarding this application should be directed to the attention of the undersigned at Mylan Pharmaceuticals Inc., P.O. Box 4310, 781 Chestnut Ridge Road, Morgantown WV, 26504-4310.

Sincerely,

J M. Ag For

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

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SEP 30 1997
GENERIC DRUGS

Department—Fax Numbers

Accounting	(304) 285-6403	Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Administration	(304) 599-7284	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
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		Medical Unit	(304) 598-5445		