CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

74975

CHEMISTRY REVIEW(S)

DIVISION REVIEW SUMMARY

ANDA 74-975 **DRUG PRODUCT:** Acyclovir

FIRM: Ranbaxy Pharmaceuticals, Inc.

U.S. Agent for: Ranbaxy Laboratories Limited

DOSAGE FORM: Capsules (Oral) **STRENGTH:** 200 mg

CGMP STATEMENT/EIR UPDATE STATUS: ACCEPTABLE -
An **ESTABLISHMENT EVALUATION REQUEST** issued 10/10/96 to the Division of Compliance has found the CGMP status of the facilities acceptable, dated 12/17/97.

BIO INFORMATION: Satisfactory -
The Division of Bioequivalence has found the bio study acceptable. See review of bio amendment dated May 1, 1998.

VALIDATION-(DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S): Pending -
Methods validation is required on the drug product because it is a non compendial item. Methods validation is not required for the drug substance. Methods validation found acceptable dated 7/7/98, as for the Detroiot District Laboratory.

STABILITY: Satisfactory -
Accelerated (40°C/75% RH)) stability data are provided from lot no. D20511 tested initially, 1, 2 and 3 months. The lot was packaged in 100 count (lot #D20511M) and 500 count (lot #20511N) bottles in the final marketed container/closure systems. The data are adequate and within the specified limits. The revised stability protocol is adequate and provides the requested information. The container/closure systems used in the stability studies are the same as those in the container section of the application. An expiration dating of 24 month has been granted.

LABELING: Acceptable
See review of professional labeling conducted by Chan Park, concurred by Charlie Hoppes, dated 8/21/98.

STERILIZATION VALIDATION: N/A

SIZE OF BIO BATCH (FIRM'S SOURCE OF NDS OK?) Satisfactory -
Lot #D20511 (RANBAXY LABORATORIES LIMITED NDS lot #DAC-00295) is a capsules (theoretical) production batch, actual yield capsules. DMF was found satisfactory, dated 8/27/98.

SIZE OF STABILITY BATCHES - Satisfactory -
Lot no. D20511, theoretical production batch size capsules, actual yield capsules. Total packaged: capsules. From the batch capsules were packaged in blister pak of 10s. Applicant does not intend to market this package size. The packaging reconciliation for batch = % (pp 007-035). The entire batch was packaged. The batch was manufactured using production scale equipment under production conditions. The batch size meets the Office of Generic Drug policy #22-90 which requires a minimum units batch or % of the proposed production batch size, whichever is greater.

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?

The proposed production batch size is capsules (Sec. XI, pp. 007-035). The manufacturing process is the same as for lot #D20511.

RECOMMENDATION:

APPROVE

1. CHEMIST'S REVIEW NO. 2

2. ANDA 74-975

3. NAME AND ADDRESS OF APPLICANT
Ranbaxy Laboratories Limited
19 Nehru Place, New Delhi, India

U.S. Agent:
Shirley Terynik
600 College Road East
Princeton, NJ 08540

4. LEGAL BASIS FOR ANDA SUBMISSION
Generic version of Burroughs Wellcome's ZOVIRAX®
(NDA 18-828). Patent certification and exclusivity statement are provided (Vol. 1.1, Section III, pp. 001-007).

Final approval date is January 25, 1985.

U.S. Patent No. 4,199,574 expired April 22, 1997

5. SUPPLEMENT(s) N/A

6. ESTABLISHED NAME
Acyclovir Capsules

7. PROPRIETARY NAME
Zovirax®

8. SUPPLEMENT(s) PROVIDE(s) FOR Original ANDA

9. AMENDMENTS AND OTHER DATES

Firm		**FDA**
Orig. submission	10/09/96	Acknowledgment letter 12/04/96
New Correspondence	10/21/96	CSO review 11/19/96
New correspondence	11/25/96	Labeling review 01/29/97
		Bioequivalency 03/25/97
		Bio deficiency letter 04/03/97
New Correspondence	5/23/97	Method validation 07/07/97

New correspondence	5/26/97	Deficiency letter 06/09/97
Amendment (Bio) 05/19/98	1/9/98	Bio review
Amendment (Chem)	3/26/98	Labeling review 09/08/98
Fax Amendment (labeling)	7/22/98	
Fax Amendment	8/24/98	

This review covers submission dated March 26, 1998.

10. PHARMACOLOGICAL CATEGORY
Indicated for the treatment of initial episodes and management of recurrent episodes of genital herpes in certain patients and for the acute treatment of herpes zoster (shingles) and chickenpox (varicella).

11. Rx or OTC
℞

12. RELATED DMF(s)
DMF

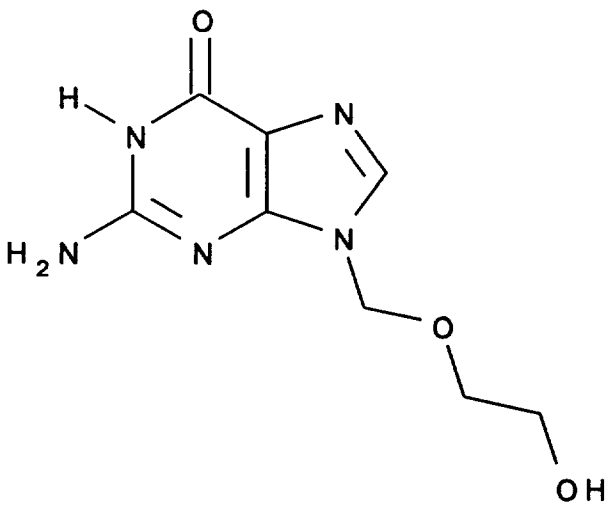
13. DOSAGE FORM
Capsules **(GELATIN)**

14. STRENGTH
200 mg

15. CHEMICAL NAME AND STRUCTURE

Acyclovir USP

$C_8H_{11}N_5O_3$; M.W. = 225.21



9-[(2-Hydroxyethoxy)methyl]guanine. CAS [59277-89-3]

Drug substance is an official USP 23 item. Drug product is not an official USP 23 item.

16. RECORDS AND REPORTS None

17. COMMENTS

a. Application is satisfactory for approval
b. Labeling is **Acceptable dated 8/21/98.**
c. Bio is **ACCEPTABLE**, dated 5/19/98
d. DMF is **ADEQUATE**, dated 8/27/98.
e. Methods validation for drug product has been submitted to the Detroit Regional Laboratory, dated 3/26/97, and found acceptable 7/7/97.
f. Drug Substance does not require Methods validation
g. Establishment evaluation submitted to compliance, dated 10/31/96, and found acceptable 12/17/97.

18. CONCLUSIONS AND RECOMMENDATIONS

APPROVE

19. REVIEWER: Raymond Brown

DATE COMPLETED: June 16, 1998