CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40-009

CHEMISTRY REVIEW(S)

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Chemistry Division II - Branch VI
Abbreviated New Drug Application Review

1. CHEMIST'S REVIEW NO. 5

2. ANDA # 40-009

3. NAME AND ADDRESS OF APPLICANT
Inwood Laboratories, Inc.
909 Third Avenue
New York, New York 10022-4731

4. LEGAL BASIS for ANDA SUBMISSION
Isordil® Tembids® 40 mg CR Tablets
Wyeth-Ayerst Laboratories
P.O. Box 8299
Philadelphia, PA 19101

Federal Register (August 3, 1984, page 31151, Docket No. 77N-0240, DESI 1786).

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME

7. NONPROPRIETARY NAME
Isosorbide Dinitrate USP

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:
Firm:

4/4/91	Original Submission.
4/26/91	Amendment - Address of suppliers.
10/25/91	Amendment - Correct Master Formula for amount of Colloidal Silicon Dioxide.
5/11/92	Amendment - Response to Agency letter, 10/28/91.
12/15/93	Amendment - Response to Bioequivalence letter of 4/29/92.
4/15/95	Amendment - Submission of Bioequivalence Study.
8/18/95	Amendment - Response to Agency letter of 7/6/92.
9/11/97	Amendment - Response to Agency letter of 8/18/95.
11/2/98	Telephone Amendment - Withdraw of Zeneca as Drug Substance source.
11/25/98	Tele-phone Amendment - Response to request of 11/25/98.

FDA:

4/4/91	Receipt acknowledged.
10/28/91	Issuance of Not Approvable letter.
4/29/92	Issuance of Bioequivalence deficiency letter.
7/6/92	Issuance of Not Approvable letter.
3/15/94	Issuance of Bioequivalence deficiency letter.
4/4/96	Issuance of Not Approvable letter.
10/27/98	Telephone Amendment.
11/25/98	Telephone Amendment.

10. PHARMACOLOGICAL CATEGORY
Vasodilator

11. Rx or OTC
Rx

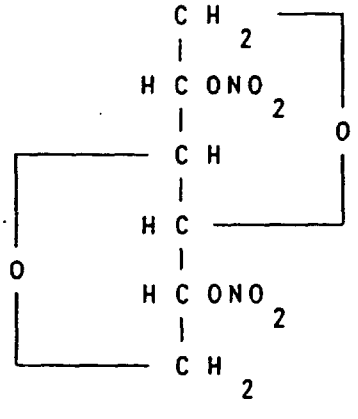
12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM
Extended Release
Tablet

14. POTENCY
40 mg

15. CHEMICAL NAME AND STRUCTURE

Isosorbide Dinitrate USP
$C_6H_8N_2O_8$; M.W. = 236.14



D-Glucitol, 1,4:3,6-dianhydro-, dinitrate
CAS [87-33-2]

Hard, colorless crystals, mp 70°C, optical rotation +135° in alcohol. Sparingly soluble in water (1.089 mg/mL), freely soluble in organic solvents such as acetone, alcohol, ether.

16. RECORDS AND REPORTS

7/30/91 - Labeling review, M. Jones.
9/18/91 - Recommendation to withhold approval, Office of Compliance.
9/19/91 - Chemistry review #1, M. Shih.
4/6/92 - Bioequivalence review, A.J. Jackson.
5/20/92 - Labeling review, M. Jones.
6/16/92 - Chemistry review #2, G.J. Smith.
8/17/92 - Methods Validation Report, New York Regional Laboratory.
3/5/94 - Bioequivalence review, A.J. Jackson.
2/17/96 - Bioequivalence review, A.J. Jackson.
3/7/96 - Labeling review, A.Vezza.
7/28/96 - Chemistry review #3, G.J. Smith.
11/5/97 - Chemistry review #4, G.J. Smith.

17. COMMENTS

The firm has resolved all major questions concerning the chemistry, manufacturing, and controls section of the application.

Labeling was found to be satisfactory.

Bioequivalence studies were found to be satisfactory by the Division of Bioequivalence.

An acceptable EIR was issued by the Office of Compliance.

The Methods Validation was found to be acceptable.

The DMF's for the drug substance were found to be satisfactory.

18. CONCLUSIONS AND RECOMMENDATIONS

The application may be Approved.

19. REVIEWER: DATE COMPLETED:

Glen Jon Smith

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Contain Trade Secret,

Commercial/Confidential

Information and are not

releasable.

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