CENTER FOR DRUGEVALUATION AND RESEARCH

APPLICATION NUMBER 75041

CHEMISTRY REVIEW(S)

Page(s) 4

Contain Trade Secret,

Commercial/Confidential

Information and are not

releasable.

Revised Review 8/6/97

#38

Page(s) 3

Contain Trade Secret,

Commercial/Confidential

Information and are not

releasable.

Chemist Review
8/26/98

#3P

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-041 APPLICANT: Élan Pharmaceutical Research Corporation

DRUG PRODUCT: Isosorbide Mononitrate Extended-release Tablets (60 mg)

The deficiencies presented below are based on our review of your April 16, 1998 minor amendment:

Deficiencies:

1. When statistical evidence shows a blend analysis is no longer necessary, please confirm that you will submit a supplement under 314.70(b)(2)(iv) prior to deleting the test.

2. Originally you indicated that your acceptance criterion for the blend analysis was of label claim. In your amendment dated April 16, 1998 you further clarify that the mean assay value must be between but all individual values must be between ith an RSD of NMT In essence you are using content uniformity criteria for the blend. We feel these criteria are inappropriate, and that each individual sample should at least meet compendial assay limits of 90-110%. In addition we feel an RSD of 4-5% is a more appropriate limit on variation in the blend. Please reconsider your proposed criteria.

Please respond to these comments as soon as possible and designate in your cover letter that the response is a "Minor Telephone Amendment". A copy may be Faxed to 301-443-3839 to the attention of Mark Anderson. Two hard copies should be sent to the application.

OFFICE OF GENERIC DRUGS
CHEMISTRY, MANUFACTURING AND CONTROLS REVIEW

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1. **CHEMIST'S REVIEW NO.** 3

2. **ANDA#** 75-041

3. **NAME AND ADDRESS OF APPLICANT**
Élan Pharmaceutical Research Corporation
1300 Gould Drive
Gainesville, GA 30504

4. **LEGAL BASIS FOR ANDA SUBMISSION**
The application is based on the reference listed drug **IMDUR®** manufactured by Schering Plough (NDA 20-225). A signed patent certification was provided along with an exclusivity statement. Exclusivity as a new chemical entity expired on 12/30/96.

5. **SUPPLEMENT(s)**
N/A

6. **PROPRIETARY NAME**
N/A

7. **NONPROPRIETARY NAME**
Isosorbide Mononitrate Extended-release Tablets 60 mg

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

9. **AMENDMENTS AND OTHER DATES**
Firm:
Original Submission: 12/31/96
New Correspondence: 6/2/97
Amendment (Major): 11/13/97
Amendment (Minor): 4/16/98
Amendment (Telephone): 5/8/98
Amendment (Telephone): 7/30/98

FDA:
Acceptance to File: 2/24/97
Fax Deficiencies (Chemistry/Labeling): 8/6/97
Fax Deficiencies (Bio): 12/16/97
Fax Deficiencies (Chemistry/Labeling): 3/26/98
Telephone Fax (Chemistry): 4/29/98

Fax Deficiencies (Bio): 6/15/98
Fax Deficiencies (Bio): 7/23/98
Fax Deficiencies (Bio): 7/29/98

10. **PHARMACOLOGICAL CATEGORY**
Vasodilator (coronary)

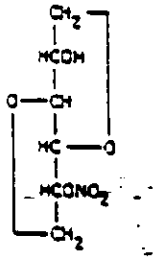
11. **HOW DISPENSED**
Rx

12. **RELATED IND/NDA/DMFs**

13. **DOSAGE FORM/ROUTE OF ADMINISTRATION**
Extended-release Tablets/Oral

14. **STRENGTH**
60 mg

15. **CHEMICAL NAME AND STRUCTURE**



(1) D-Glucitol,1,4:3,6-dianhydro-,5-nitrate;
(2) 1,4:3,6-Dianhydro-D-glucitol 5-nitrate.

$C_6H_9NO_6$
Molecular Weight: 191.14

16. **RECORDS AND REPORTS**
N/A

17. **COMMENTS**
This application represents a "first generic" for this drug product. All CMC issues have been resolved and tentative dissolution specifications have been approved by the Division of Bioequivalence. The methods validation package was prepared and issued on 8/4/98. The EER and labeling are acceptable.

18. **CONCLUSIONS/RECOMMENDATIONS**
Recommend approval

19. **REVIEWER** S. M. Rosencrance
Susan Rosencrance 8/6/98

DATE COMPLETED
5/12/98; updated 5/29/98; updated 8/4/98