

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

74496

CHEMISTRY REVIEW(S)

ANDA APPROVAL SUMMARY

ANDA: 74-496

DRUG PRODUCT: Lorazepam Injection USP

FIRM: Elkins-Sinn Pharmaceuticals, div. American Home Product

DOSAGE FORM: Injection

STRENGTH: 2 mg/mL and 4 mg/mL (Dosette®
Cartridge Syringes)

CGMP: EER is acceptable (OC recommendation, 8/4/98).

BIO: A bio waiver has been granted (Hoainhon Nguyen, 9/29/94)

VALIDATION -(DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):

The drug substance and drug product are compendial monographs in the US Pharmacopeia.

STABILITY:

The containers in the stability study are identical to those in the container section.

LABELING:

Container, carton and insert labeling have been approved (L. Golson, 7-29-96 and update review 4/30/98).

STERILIZATION VALIDATION (IF APPLICABLE):

Sterile drug product. The sterility portion of this application has been reviewed and found to be satisfactory (J. McVey, 8-9-96). The amendment of Sept 3, 1997 and Oct 16, 1997 were found to be satisfactory (J. McVey, 11/17/97).

SIZE OF BIO BATCH (FIRM'S SOURCE OF NDS OK?):

The proposed production batch sizes for Lorazepam Injection are:

Lorazepam Injection, 2 mg/mL	L
Lorazepam Injection, 4 mg/mL	L.

The size of the executed exhibit batches were liters for the 2 mg/mL strength (Lot #P123296) and liters for the 4 mg/mL strength (Lot #P123282), the same sizes as the proposed production batches.

The Drug Master File for the drug substance is currently adequate (reviewed by Liang-Lii Huang, Ph.D., 4/30/98).

SIZE OF STABILITY BATCHES- (IF DIFFERENT FROM BIO BATCH, WERE THEY MANUFACTURED VIA THE SAME PROCESS?):

The exhibit batches are the bio batches. Bio waiver approved.

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME?:

The proposed production batch sizes for Lorazepam Injection are:

Lorazepam Injection, 2 mg/mL	L
Lorazepam Injection, 4 mg/mL	L.

CHEMIST: Liang-Lii Huang, Ph.D.
SUPERVISOR: P. Schwartz, Ph.D.

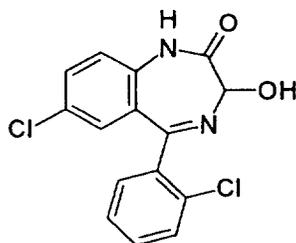
DATE: August 21, 1998
DATE: August 21, 1998

OFFICE OF GENERIC DRUGS
CHEMISTRY, MANUFACTURING AND CONTROLS REVIEW

1. CHEMIST'S REVIEW NO. six (6)
2. ANDA # 74-496
3. NAME AND ADDRESS OF APPLICANT

Elkins-Sinn Pharmaceuticals
Division of American Home Product Company
Attention: Mark Bokelman
2 Esterbrook Lane
Cherry Hill, NJ 08003-4099
4. LEGAL BASIS OF SUBMISSION:
Ativan® (Wyeth's, Reference Listed Drug)
Existing Patent, Patent No 4017616 expires on 4-12-94.
No exclusivity
5. SUPPLEMENT(s)
N/A
6. PROPRIETARY NAME
N/A
7. NONPROPRIETARY NAME
Lorazepam Injection USP, 2 mg/mL and 4 mg/mL (Dosette®
Cartridge Syringes)
8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A
9. AMENDMENTS AND OTHER DATES:
Applicant:
05-06-1994 Original Submission
05-24-1994 Amendment (Exclusivity statement)
03-29-1995 Amendment (Micro amendment)
04-20-1995 Amendment (containers withdrawn)
04-24-1995 Amendment
05-03-1995 Amendment (correction of deficiency comment)
07-17-1996 Amendment (Minor)
10-15-1996 Amendment (Minor)
09-03-1997 Amendment
10-16-1997 Amendment
04-20-1998 Amendment
06-12-1998 Amendment (telephone amendment)
06-26-1998 Amendment (telephone amendment)
08-06-1998 Amendment
FDA:
05-19-1994 Refuse to file
06-09-1994 Acknowledgement Letter
01-13-1995 NA Letter
11-13-1995 NA Letter (Minor)
08-28-1996 NA Letter (Minor)
10. PHARMACOLOGICAL CATEGORY

- Sedative ; relieves anxiety (anxiolytic)
11. Rx or OTC
Rx
 12. RELATED IND/NDA/DMF(s)
Listed Drugs: Ativan®
Holder: Wyeth Laboratories
NDA: #18-140
For DMF's details please refer to item of this review.
 13. DOSAGE FORM
Solution (Injectable)
 14. STRENGTH
2 mg/mL and 4 mg/mL (Syringe)
 15. CHEMICAL NAME AND STRUCTURE
Lorazepam. 2H-1,4-Benzodiazepin-2-one, 7-chloro-5-(2-chlorophenyl)-1,3-dihydro-3-hydroxy-, (±)-. C₁₅H₁₀Cl₂N₂O₂.
321.16. 846-49-1. Tranquilizer (minor). USP 23, page 903.



16. COMMENTS
None
 17. CONCLUSIONS AND RECOMMENDATIONS
This application is approvable.
 18. RECORDS AND REPORTS
N/A
 19. REVIEWER:
Liang-Lii Huang, Ph.D.
Endorsed by P. Schwartz, Ph.D.
- | |
|------------------------|
| <u>DATE COMPLETED:</u> |
| August 20, 1998 |
| August 20, 1998 |