

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER 74941**

**CHEMISTRY REVIEW(S)**

1. CHEMISTRY REVIEW NO. 3

2. ANDA #: 74-941

3. NAME AND ADDRESS OF APPLICANT

Abbott Laboratories  
Attention: David T. Guzek  
200 Abbott Park Road D-389, AP30  
Abbott Park, IL 60064

4. LEGAL BASIS FOR SUBMISSION

The listed drug is Cardizem® Injectable (5 mg/mL) held by Hoechst Marion Roussel (formerly Marion Merrell Dow), NDA 20-027.

Sanofi Winthrop states that the patent for Cardizem® Injectable is expired and is not entitled to a period of marketing exclusivity under Section 505(j)(4)(D) of the Act.

A patent certification and exclusivity statement is included in the submission.

5. SUPPLEMENT(s): N/A

6. PROPRIETARY NAME: N/A

7. NONPROPRIETARY NAME  
Diltiazem Hydrochloride

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

9. AMENDMENTS AND OTHER DATES:

Firm:

Submitted: August 13, 1996  
Amendment (Packaging/yield): September 27, 1996  
New Correspondence (Ownership transfer): June 18, 1997  
Amendment: October 7, 1997  
Fax amendment: January 22, 1998  
Amendment (Label): March 18, 1998

FDA:

Memo (Refuse to File): September 9, 1996  
Letter (Refuse to File): September 20, 1996  
Letter (Acknowledgment): October 18, 1996  
Micro review: January 8 & 21, 1997  
Bio (letter/review): January 23, 1997  
Chem Rev # 1 & FAX: May 14, 1997  
Chem rev # 2 & FAX: December 22, 1997

10. PHARMACOLOGICAL CATEGORY  
Calcium ion influx inhibitor

11. Rx or OTC  
Rx

12. RELATED IND/NDA/DMF(s)

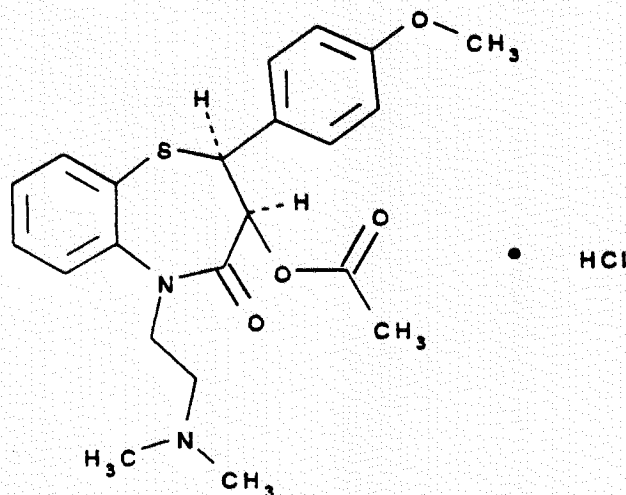
13. DOSAGE FORM  
SVP (Injection)

14. POTENCY  
5 mg/mL

15. CHEMICAL NAME AND STRUCTURE

Diltiazem Hydrochloride USP

$C_{22}H_{26}N_2O_4 \cdot HCl$ ; M.W. = 450.98



(+)-5-[2-(Dimethylamino)ethyl]-*cis*-2,3-dihydro-3-hydroxy-2-(*p*-methoxyphenyl)-1,5-benzothiazepin-4(5H)-one acetate (ester) monohydrochloride. CAS [33286-22-5]

16. RECORDS AND REPORTS: N/A

17. COMMENTS

- Ownership of this ANDA was transferred to Abbott Labs - 6/18/97.
- Labeling satisfactory 3/26/98.
- Bio waiver granted 1/17/97.
- Chemistry, manufacturing and controls procedures are satisfactory 1/28/98.
- Microbiological review satisfactory 2/6/98.
- EIR is acceptable - 3/26/97.

18. CONCLUSIONS AND RECOMMENDATIONS

This ANDA can be approved.

19. REVIEWER:

Donald Shostak

DATE COMPLETED:

January 28, 1998

(Revised - labeling 3/26/98)

1. CHEMISTRY REVIEW NO.: 2

2. ANDA #: 74-941

3. NAME AND ADDRESS OF APPLICANT

Abbott Laboratories  
Attention: David T. Guzek  
200 Abbott Park Road D-389, AP30  
Abbott Park, IL 60064

4. LEGAL BASIS FOR SUBMISSION

The listed drug is Cardizem® Injectable (5 mg/mL) held by Hoechst Marion Roussel (formerly marion Merrell Dow), NDA 20-027.

Sanofi Winthrop states that the patent for Cardizem® Injectable is expired and is not entitled to a period of marketing exclusivity under Section 505(j)(4)(D) of the Act.

A patent certification and exclusivity statement is included in the submission.

5. SUPPLEMENT(s): N/A

6. PROPRIETARY NAME: N/A

7. NONPROPRIETARY NAME  
Diltiazem Hydrochloride

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

9. AMENDMENTS AND OTHER DATES:

Firm:

Submitted: August 13, 1996  
Amendment (Packaging/yield): September 27, 1996  
New Correspondence (Ownership transfer): June 18, 1997  
Amendment: October 7, 1997

FDA:

Memo(Refuse to File): September 9, 1996  
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Chem Rev # 1 & FAX: May 14, 1997

10. PHARMACOLOGICAL CATEGORY  
Calcium ion influx inhibitor

11. Rx or OTC  
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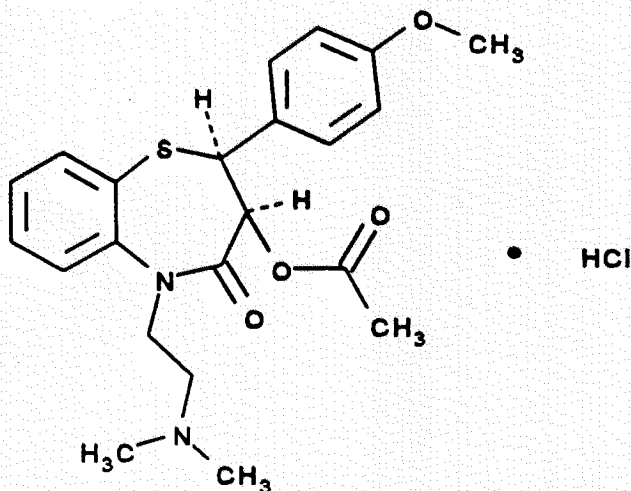
12. RELATED IND/NDA/DMF(s)

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16. RECORDS AND REPORTS: N/A

17. COMMENTS

- a. Ownership of this ANDA was transferred to Abbott Labs - 6/18/97.
- b. Labeling is unsatisfactory - 10/30/97.
- c. Bio waiver granted 1/17/97.
- d. Deficiencies remain in regard to the methods validation.
- e. Microbiological review of the 10/7/97 amendment is pending as of 11/5/97.
- f. EIR is acceptable - 3/26/97.
- g. The lab conclusions regarding the methods validation were that the methods will be acceptable with modification. See item 31 of this review.

18. CONCLUSIONS AND RECOMMENDATIONS

This ANDA is NOT APPROVABLE. The amendment will be MINOR.

19. REVIEWER:

Donald Shostak

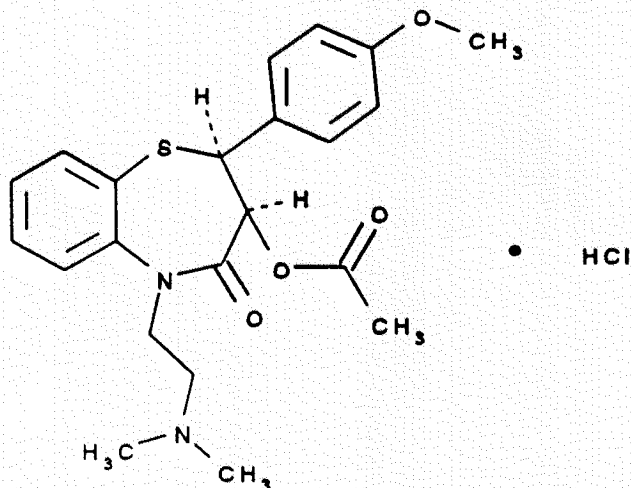
DATE COMPLETED:

November 12, 1997

1. CHEMISTRY REVIEW NO.: 1
2. ANDA #: 74-941
3. NAME AND ADDRESS OF APPLICANT  
Sanofi Winthrop, Inc  
Attention: Gregory M. Torre, Ph.D., J.D.  
90 Park Avenue  
New York, NY 10016-1389
4. LEGAL BASIS FOR SUBMISSION  
The listed drug is Cardizem® Injectable (5 mg/mL) held by Hoechst Marion Roussel (formerly marion Merrell Dow), NDA 20-027.  
  
Sanofi Winthrop states that the patent for Cardizem® Injectable is expired and is not entitled to a period of marketing exclusivity under Section 505(j)(4)(D) of the Act.  
  
A patent certification and exclusivity statement is included in the submission.
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6. PROPRIETARY NAME: N/A
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16. RECORDS AND REPORTS: N/A

17. COMMENTS

- a. Minor chemistry deficiencies remain
- b. Label review is unsatisfactory 2/21/97
- c. Microbiological review is unsatisfactory 1/8/97
- d. Bio waiver granted 1/17/97
- e. Label review pending
- f. EIR pending
- g. Methods validation on the drug product is pending

18. CONCLUSIONS AND RECOMMENDATIONS

This ANDA is NOT APPROVABLE. The amendment will be MINOR.

19. REVIEWER:

Donald Shostak

DATE COMPLETED:

March 5, 1997