CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40309

CHEMISTRY REVIEW(S)

DIVISION REVIEW SUMMARY

ANDA: 40-309

FIRM: Barr Laboratories, Inc.
2 Quaker Road
P.O. Box 2900
Pomona, NY 10970-5019

DOSAGE FORM: Tablet STRENGTH: 10 mg/500 mg

DRUG: Hydrocodone Bitartrate and Acetaminophen

CGMP STATEMENT/EIR UPDATE STATUS: Acceptable 11/16/98

BIO STUDY INFORMATION: Bio waiver granted. In-vitro dissolution data found acceptable on 8-6-98.

METHODS VALIDATION:

Active drug substance and drug dosage forms are both compendial items per USP 24.

STABILITY:

The containers used in the stability study are of the same size and material as those described in the container section. The firm submitted accelerated stability data for the product packaged in all container sizes.

The firm requests an expiration date of 24 months based on the data submitted.

The stability tests and specifications are as follows:

Product description and physical characteristics:

10 mg/500 mg:

Description: Light beige mottled, capsule-shaped, scored tablets. Debossed with b/919 on one side and plain on the other side

Dissolution:

a. Hydrocodone Bitartrate:
pH 5.8 buffer, 900 mL, USP 2, 50 rpm, assay, NLT % dissolved in 30 mins.

b. Acetaminophen:
pH 5.8 buffer, 900 mL, USP 2, 50 rpm, assay, NLT [redacted] % dissolved in 30 mins.

Assay:

[redacted]

Impurities/degradants:

[redacted]

[redacted]

LABELING: Acceptable.

STERILIZATION VALIDATION: N/A

SIZE OF BIO BATCH:

Bio-waiver was granted based on in-vitro dissolution data obtained on the exhibit batch.

SIZE OF STABILITY BATCHES:

The executed batch records can be found on the following pages:

10 mg/500 mg:

a. [redacted] (executed batch #7T91901), p.12-0004-12-00115)
b. [redacted](blank batch record), p. 11-00010-11-00064

PROPOSED PRODUCTION BATCH:

The proposed production batch size is [redacted]

RECOMMENDATION: Approve.

SIGNATURE: /S/
/S/

DATE: 7/24/00
7/25/00

Redacted 3

pages of trade

secret and/or

confidential

commercial

information

Specs

1. CHEMISTRY REVIEW NO. 3

2. ANDA # 40-309

3. NAME AND ADDRESS OF APPLICANT
Barr Laboratories, Inc.
Attention: Christine Mundkur
2 Quaker Road
P.O. Box 2900
Pomona, NY 10970-5019

4. LEGAL BASIS FOR SUBMISSION
UCB Pharma Inc. - Lortab® 10 mg/ 500 mg (40-100)

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Hydrocodone Bitartrate and Acetaminophen Tablets USP

9. AMENDMENTS AND OTHER DATES:
Firm :
4-15-98: Original application
7-13-99: Amendment
4-12-00: Amendment
7-11-00: tele-amendment

FDA:
5-21-98: acknowledgement
1-18-00: NA Letter

10. PHARMACOLOGICAL CATEGORY
Analgesic and Antitussive

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM
Tablet

14. POTENCY
10 mg/500 mg

15. CHEMICAL NAME AND STRUCTURE
Acetaminophen:
C8H9NO2 M.W. 151.16
Chemical name: Acetamide, N-(4hydroxyphenyl)-4'-Hydroxyacetanilide

Hydrocodone Bitartrate:

C18H21NO3.C4H6O6.2H2O M.W. 494.5
Morphinan-6-one, 4,5-epoxy-3-methoxy-17-methyl,(5a)-,[R-(R*,*)]-2,3-dihydroxybutanedioate(1:1), hydrate(2:5).
4,5a-Epoxy-3methoxy-17-methylmorphinan-6-one tartrate(1:1) hydrate (2:5).
Anhydrous 449.46

17. COMMENTS
Status:

a. **EER: Acceptable**

Requested for Barr Laboratories Inc. (Forest, VA, Northvale, NJ and Pomona, NY), [ ]by T, Ames on 5/21/98. AC 11/16/98.

Note: A summary of the findings from the initial inspection were submitted in a memo from Compliance dated November 17, 1998. The investigator included a note to the chemist expressing concern over the lack of validation for determination of impurities in the [ ]The review chemist has determined that the applicant conducts testing for the the major known impurities in both the[ ]and final drug product. Method descriptions and validation data have been provided.

b. MV (method validation): **Acceptable**

Active drug substance and drug dosage form are both compendial items per USP 23. Samples will not be requested for testing by FDA labs.

c. Bio-Review: Acceptable

Acceptable per Z. Wahba reviewed on 8-5-98.

d. Labeling review: Acceptable

Satisfactory per Park 11/10/99.

e. DMFs: Satisfactory

DMF[ ]for Acetaminophen, USP was reviewed by A.Langowski and found satisfactory on 4/27/00.
DMF[ ]for Hydrocodone Bitartrate was reviewed by

Langowski and found satisfactory on 07/24/00.

18. CONCLUSIONS AND RECOMMENDATIONS
Approval.

19. REVIEWER: Andrew J. Langowski
DATE COMPLETED: 6/09/00; 7/19/00