CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40276

CHEMISTRY REVIEW(S)

DIVISION REVIEW SUMMARY

ANDA: 40-276

DRUG PRODUCT: Phentermine Hydrochloride

FIRM: Purepac

DOSAGE FORM: Tablets

STRENGTHS: 37.5 mg

CGMP STATEMENT/EIR UPDATE STATUS: Acceptable 4/23/98

BIO INFORMATION: Acceptable 1/9/98 by M. Makary.

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

Page 738 contains a Certificate of Analysis for the finished product (exhibit batch #PI-985). Testing includes:

Test	Specification
Description	Meets description
Identification	
A. USP 23	IR spectrum matches
B. In-house	LC retention time matches
Uniformity of Dosage Units USP <905>	%
*Moisture KF	NMT %
**Related Compounds	NMT % for each known impurity
In-House Method	NMT % for any unknown impurity
	NMT % total
Dissolution USP <711>	NLT %(Q) of label in 45 minutes
Assay In-House method	% of label

*Added upon request, recently lowered upon request.

**Revised upon request¶. The firm utilizes a modification of the Phentermine Hydrochloride Capsules, USP method. (The USP assay method for tablets is not stability indicating, and the firm has modified the USP capsule method which was found to be stabilty indicating. This method has also been used by other firm's and the USP has recently acknowledged that this method will be acceptable in a future PF).

The firm utilizes their own in-house method for assay and related compounds which is an method using current methodologies of the USP 23 with some modifications. The firm performed forced degradation studies with the method using . The firm concluded that their assay method for stability using was stability indicating. The firm acknowledges that the USP method is the regulatory standard and if a dispute should occur, the USP method is considered the preferred method.

STABILITY-

The firm includes the stability specifications on pages 1070-1071. Tests that will be performed will include: Visual (meets description), Physical examination (in-house), *Related Compounds NMT % for each known impurity, NMT % for each unknown, NMT % total impurities (revised upon request), Dissolution USP 23 NLT % (Q) in 45 minutes of label,and Assay % of label. **Moisture (KF) NMT % was added upon request. Room temperature studies will be performed at 25°-30°C, ambient humidity. Accelerated studies were performed at 40°C, 75% RH. As mentioned above, methods were found to be stability indicating.

Included are data from exhibit batch #PI-985. Data from the 100 CRC Tablets 100 non-CRC tablets, and the 1000 unit non-CRC fill were included as well as the bulk. Both room temperature and accelerated (40° C, 75% RH) data were included, except the bulk, which included 3 months of room temperature data only.

The firm proposes a 2 year expiration period initially. A post approval stability commitment is included on page 1099.

LABELING-The labeling review was found satisfactory as of 9/2/98 by K. Lee.

STERILIZATION VALIDATION - Not Applicable

SIZE OF BIO BATCHES-
A description of the manufacturing process is included beginning on page 275. The process involves

A list and comparison of the equipment is included. Also included are 3 sets of blank batch records for intended production of tablets, tablets and tablets beginning on page 275. The executed batch records are included on beginning on page 365. The exhibit batch size was tablets for lot #PI-985. The batch records state that the batch was manufactured on 4/9/97, although it appears to have been manufactured over the course of several days. The % accountable yield for the pre-blend was reported as %, for the milled blend it was reported as % and for the final blend it was reported as %. The total accountable yield of compression was reported as %. The theoretical % yield for the batch was reported as %. The firm manufactured tablets and packaged units in accordance with OGD PPG #41-95. A % percent packaging accountability was included. The firm also submitted data from a developmental batch (size for lot #PI-989.

SIZE OF STABILITY BATCHES- same as above

PROPOSED PRODUCTION BATCH- See above
tablets).

RECOMMENDATION: The application is approvable.

SIGNATURE: /S/ DATE: 11/12/98
Karen Bernard, Ph.D. 11/2/98

1. CHEMISTRY REVIEW NO 4

2. ANDA 40-276

3. NAME AND ADDRESS OF APPLICANT

Purepac Pharmaceutical Company
Attention: Joan Janulis
200 Elmora Avenue
Elizabeth, NJ 07207

4. LEGAL BASIS FOR SUBMISSION
The firm includes a patent certification statement on page 008 and a basis for ANDA submission on page 006.

5. SUPPLEMENT(s)
NA

6. PROPRIETARY NAME
ADIPEX-P

7. NONPROPRIETARY NAME
Phentermine Hydrochloride, USP

8. SUPPLEMENT(s) PROVIDE(s) FOR:
NA

9. AMENDMENTS AND OTHER DATES:
Original Submission September 11, 1997
FDA acknowledgement letter September 26, 1997
FDA Deficiency Letter January 27, 1998
Amendment Response February 13, 1998
FDA Minor Deficiency Letter July 21, 1998
Amendment Response August 20, 1998
FDA Fax Deficiency Letter October 16, 1998
*Amendent Response October 26, 1998

10. PHARMACOLOGICAL CATEGORY
Anorexic

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)
DMF
DMF
DMF
DMF
DMF
DMF
DMF
DMF
DMF

DMF
DMF
DMF
DMF
DMF
DMF

13. DOSAGE FORM
Tablets

14. POTENCY
37.5 mg

15. CHEMICAL NAME AND STRUCTURE
Benzeneethanamine, alpha, alpha,-dimethyl-, hydrochloride.

16. RECORDS AND REPORTS
NA

17. COMMENTS
All deficiencies have been resolved satisfactorily.

18. CONCLUSIONS AND RECOMMENDATIONS
This application is approvable.

19. REVIEWER:
Karen A. Bernard, Ph.D.

DATE COMPLETED:
11/3/98

Redacted 20

pages of trade

secret and/or

confidential

commercial

information

Chemistry Review #4