CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-796

CHEMISTRY REVIEW(S)

FEB 13 2001

38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-796 APPLICANT: Duramed Pharmaceuticals, Inc.

DRUG PRODUCT: Levonorgestrel and Ethinyl Estradiol Tablets, USP 0.10 mg/0.02 mg

The deficiencies presented below represent FAX deficiencies.

A. Deficiencies:

1. In the 09/15/00 amendment, you provided revised specifications for the drug substances, Levonorgestrel, USP and Ethinyl Estradiol, USP. Please provide revised COAs for the lots of the two raw materials used in the manufacture of the executed batch of the drug product tested per your revised specifications.

2. Since your finished product release specification has been revised, please provide revised COA for the ANDA batch.

3. You stated that the revised finished product stability specifications were established based on evaluation of stability data accrued to date. The stability data provided on pages 053-056 of the amendment justify even a tighter specification for total impurities. Please revise the total impurities specification for finished product stability to base it on the results obtained.

4. Please revise your stability study specification for the intermediate to include testing for impurities/degradants. The acceptance criteria for this testing should be same as those established for the finished product. Also, please provide stability data for the bulk powder prep intermediate obtained per the revised specification showing the absence of impurities/degradants up to 12 months storage at room temperature condition. Alternatively, you can provide acceptable stability data for tablets compressed from the

intermediate that had been in storage at room temperature condition for at least 12 months before it was compressed into tablets.

Sincerely yours,

DS Gill

for _____
Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

Office of Generic Drugs

Chemistry, Manufacturing and Controls Review

1. CHEMISTRY REVIEW No. 3

2. ANDA **75-796 [Levonorgestrel and Ethinyl Estradiol Tablets, USP]**

3. NAME AND ADDRESS OF APPLICANT
Duramed Pharmaceuticals, Inc.
Attention: John R. Rapoza
5040 Lester Road, Cincinnati, OH 45213

4. LEGAL BASIS FOR SUBMISSION
The approved, reference listed drug Alesse™-21 Tablets, the subject of application 20-683, held by Wyeth-Ayerst, and containing 0.10 mg of Levonorgestrel and 0.02 mg of Ethinyl Estradiol.

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME
Aviane™

Note: The firm proposed the proprietary name "Aviane™ " for their product. OPDRA concluded on January 29, 2001, that "Aviane" was an acceptable name for this drug product [Consult # 00-0234].

7. NONPROPRIETARY NAME
Levonorgestrel and Ethinyl Estradiol Tablets, USP

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

9. AMENDMENTS AND OTHER DATES:

Submission date	Submission type
01/31/00	Original submission (acceptable 02/01/00)
03/07/00	Correspondence
03/10/00	Submission of EVA
03/16/00	Amendment (blank placebo batch record)
03/17/00	FDA acknowledgment letter
09/15/00	Major amendment
09/30/00	Labeling amendment
02/26/01	Amendment (This Review)
03/01/01	Amendment (This Review)
04/03/01	Telephone Amendment (This review)
04/11/01	Telephone Amendment (This Review)

10. PHARMACOLOGICAL CATEGORY Oral Contraceptive

11. Rx or OTC Rx

12. RELATED IND/NDA/DMF(s)
For DMFs see Section 37

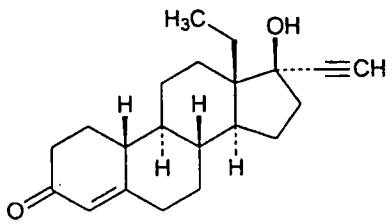
13. DOSAGE FORM Tablets

14. STRENGTH 0.10 mg/0.02 mg

15. CHEMICAL NAME AND STRUCTURE

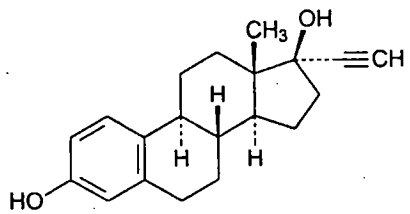
Levonorgestrel

18,19-Dinorpregn-4-en-20-yn-3-one, 13-ethyl-17-hydroxy-,(17α)-, (-)-.$C_{21}H_{28}O_2$. 312.45. 797-63-7. Progestin.



Ethinyl Estradiol

19-Norpregna-1,3,5(10)-trien-20-yne- 3,17-diol, (17α)-. $C_{20}H_{24}O_2$. 296.41. 57-36-6. Estrogen.



16. RECORDS AND REPORTS N/A

17. COMMENTS
See Review

18. CONCLUSIONS AND RECOMMENDATIONS
Approvable

19. REVIEWER:
U.S. Atwal, Ph.D.

DATE COMPLETED:
March 27, 2001

DATE REVISED:
April 6, 2001

DATE REVISED:
April 13, 2001

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Contain Trade Secret, Commercial/Confidential Information and are not releasable.

chem Rev 3
3/22/01