CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 75-256

CHEMISTRY REVIEW(S)

Addendum to Chemist's Review # 3:

ANDA 75-256 (Desogestrel and Ethinyl Estradiol Tablets)
Duramed Pharmaceuticals, Inc, OH

Approval package was prepared after completion of CR # 3. After Mike Smela sign-off, approval package went to Allen Rudman for administrative review and he found two issues which need to be resolved. These two issues are: modification of in-process blend uniformity testing specifications and stability level of impurities/degradants and for Desogestrel components of the drug product and the proposed expiration dating period of 2 years. Allen Rudman call the firm to request the telephone amendment. Duramed submitted a telephone amendment on 7-15-99 and submitted following revisions:

1. In-process blend uniformity testing:

Duramed submitted following revised in-process blend uniformity specifications deleting two-tier level testing:

The average of nine(9) samples taken from the beginning, middle and end of the discharge is 90-110% of label claim and the RSD is NMT

Acceptable per current OGD requirements regarding in-process uniformity testing.

2. Issue: The six month room temperature stability results for individual impurities on the batch S-0041 indicates that it will not meet specification of NMT t proposed 2 year expiration date. Duramed is required to submit updated stability data for this batch.

On July 15, 1999 telephone amendment, Duramed submitted updated 9 months CRT stability data and the individual unknown impurity level is which is below the . Duramed clarified that specification of : for individual impurities is reasonable at this time based on the limits manufacturing experience and available stability data clearly support their proposed two year expiration dating period.

On July 16, 1999, Allen Rudman call the firm to discuss the issue of stability of Desogestrel component which has decreased at 9 months stability station and requested additional stability data to support the stability of the drug product. On July 20, 1999, Duramed submitted the requested information. They evaluated their CRT stability samples of lot # S-0041 at 11.5 months. The assay values are reported in duplicated and they are as follows:

Component	Assay values:
Desogestrel	96.5% 96.8%
Ethinyl Estradiol	99.1% 99.1%

Duramed plotted these assay points along with previous stability values in a linear fit analysis. The outcome of this analysis for Desogestrel provided the estimated value of 91.6% of the label claim at 24 months. 3 months stability data for lot # S-0041 demonstrate that the assay value of Desogestrel component is 96.8% and assay value of · for individual impurities at 3 month stability station.

On July 21, 1998, Duramed submitted a telephone amendment to submit 11.5 months stability data and referred to linear fit analysis discussed above.

This reviewer considers that Duramed submitted adequate information to support 24 months of expiration dating period for the drug product.

Comment: Remains approved.

cc:

Endorsements:

HFD-625/M.Shaikh/ /S/ 7/21/99
HFD-625/M.Smela/ 7/21/99

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F/T by:

1. CHEMISTRY REVIEW NO. 3

2. ANDA # 75-256

3. NAME AND ADDRESS OF APPLICANT
Duramed Pharmaceuticals, Inc.
5040 Lester Road
Cincinnati, OH 45213

4. BASIS OF SUBMISSION
Listed drug product: Orth.-Cept^{R} by Johnson RW approved in NDA # 20-301.

According to patent certification, there are no active patents or periods of exclusivity in effect for the listed drug product.

The proposed drug product contains the same active ingredients and has same strength, dosage form, route of administration, indications and usage as the listed drug.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
None used.

7. NONPROPRIETARY NAME
Desogestrel and Ethinyl Estradiol Tablets

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

9. AMENDMENTS AND OTHER DATES:
FIRM:
Original submission: 11-19-97
Amendment: 12-1-97
Amendment: 1-29-98 (Response to 1-16-98)
Amendment: 2-3-98
Amendment: 2-17-98
Major Amendment: 9-17-98 (Response to 7-20-98 NA letter)
Bio amendment: 11-24-98
Amendment: 12-29-98
- Bio Amendment: 4-21-99
- Minor Amendment: 4-27-99
- Telephone amendment: 6-29-99
- Telephone amendment: 7-6-99

FDA:
Refuse to file letter: 1-16-98
Accepted for filing: 2-9-98 (Acknowledgment letter issued on 2-20-98)
NA letter: 7-20-98

Bio Deficiency letter: 8-7-98.
Bio Deficiency letter: 3-4-99
NA letter: 3-25-99

10. PHARMACOLOGICAL CATEGORY
Oral Contraceptive

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

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13. DOSAGE FORM
Tablet

14. POTENCY
21 Day: 0.15 mg/0.03 mg
28 day: 0.15 mg/0.03 mg and placebo

15. CHEMICAL NAME AND STRUCTURE
Listed in labeling insert.

16. RECORDS AND REPORTS
N/A

17. COMMENTS
1. The subject drug product contains oral contraceptive tablets supplied as active tablets only (21 day supply) or in conjunction with 7 placebo tablets (28 supply).
2. Referenced DMF for Ethinyl Estradiol is adequate per review completed by this reviewer on 3-2-99.
3. Referenced DMF # for Desogestrel is found adequate per M. Shaikh's review completed on 6-28-99.
4. A request for method validation has been requested concurrent to this review on 7-6-99.
5. Bio status became acceptable per review signed of on 5-17-99.

18. CONCLUSIONS AND RECOMMENDATIONS
Approved pending acceptable MV.

19. REVIEWER: Mujahid L. Shaikh

DATE COMPLETED: 6-11-99
Revised on 6-15-99
Revised on 6-30-99
Revised on 7-7-99

cc:

Endorsements:

HFD-625/M.Shaikh/7-7-99
HFD-625/M.Smela/7-7-99

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Chemistry, #2037, 7/99