

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

***APPLICATION NUMBER:***

**20-992/S-016**

**CHEMISTRY REVIEW(S)**

CHEMIST REVIEW #12  
OF SUPPLEMENT

1. ORGANIZATION: DRUDP HFD-580
2. NDA NUMBER: 20-992/SE1-016
3. SUPPLEMENT NUMBERS/DATES:  
Letterdate: 16-AUG-2001  
Stampdate: 17-AUG-2001
4. AMENDMENTS/REPORTS/DATES:  
Letterdate: 22-MAR-2002  
Stampdate: 25-MAR-2002
5. RECEIVED BY CHEMIST: 22-AUG-2001

6. APPLICANT NAME AND ADDRESS:

Duramed Pharmaceuticals, Inc.  
5040 Duramed Drive  
Cincinnati, OH 45213

7. NAME OF DRUG:

Cenestin Tablets

8. NONPROPRIETARY NAME:

Synthetic conjugated estrogens, A

9. CHEMICAL NAME/STRUCTURE:

The active drug substance for this product is composed of a 9 component estrogen mixture:  
See Chemistry Review #1 (11/19/98) for chemical names and structures.

10. DOSAGE FORM(S):

Tablet

11. POTENCY:

0.3, 0.625\*, 0.9\*, 1.25\* mg

\*approved strengths

12. PHARMACOLOGICAL CATEGORY:

Estrogen/Treatment of Post Menopausal Vasomotor Symptoms

13. HOW DISPENSED:

RX

14. RECORDS & REPORTS CURRENT:

Yes

15. RELATED IND/NDA/DMF:

See Chemistry Review #1.

16. SUPPLEMENT PROVIDES FOR:

Addition of a 0.3 mg dosage strength tablet.

17. SPECIAL PRODUCTS: YES \_\_\_ NO x.

(If yes, fill out the form for special products and deliver to TIA through team leader for data entry)

**18. COMMENTS**

This review is an update of the cGMP inspection outcomes. Based on the inspection of all the sites cited in this NDA including the \_\_\_\_\_ facility in \_\_\_\_\_ the Office of Compliance has issued an overall Acceptable recommendation. Therefore, from a Chemistry, Manufacturing and Controls point of view, this supplement may be approved.

**19. CONCLUSIONS AND RECOMMENDATIONS:**

From a Chemistry, Manufacturing and Controls point of view, this Efficacy Supplement for a new dosage strength tablet may be approved.

**20. REVIEWER NAME**

David T. Lin, Ph.D.  
Chemistry Team Leader

**SIGNATURE**

**DATE COMPLETED**

17-JUN-2002

cc: Original: NDA 20-992/SE1-016

HFD-580/Division File  
HFD-580/DSpellLesane  
HFD-580/DLin

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       § 552(b)(5) Deliberative Process

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/s/

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David T. Lin

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From CMC point of view, this supplement may be approved.

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CHEMIST REVIEW #1  
OF SUPPLEMENT

1. ORGANIZATION: DRUDP HFD-580
2. NDA NUMBER: 20-992/SE1-016
3. SUPPLEMENT NUMBERS/DATES:  
Letterdate: 16-AUG-2001  
Stampdate: 17-AUG-2001
4. AMENDMENTS/REPORTS/DATES:  
Letterdate: 22-MAR-2002  
Stampdate: 25-MAR-2002
5. RECEIVED BY CHEMIST: 22-AUG-2001.

6. APPLICANT NAME AND ADDRESS:

Duramed Pharmaceuticals, Inc.  
5040 Duramed Drive  
Cincinnati, OH 45213

7. NAME OF DRUG:

Cenestin Tablets

8. NONPROPRIETARY NAME:

Synthetic conjugated estrogens, A

9. CHEMICAL NAME/STRUCTURE:

The active drug substance for this product is composed of a 9 component estrogen mixture:  
See Chemistry Review #1 (11/19/98) for chemical names and structures.

10. DOSAGE FORM(S):

Tablet

11. POTENCY:

0.3, 0.625\*, 0.9\*, 1.25\* mg

\*approved strengths

12. PHARMACOLOGICAL CATEGORY:

Estrogen/Treatment of Post Menopausal Vasomotor Symptoms

13. HOW DISPENSED:

RX

14. RECORDS & REPORTS CURRENT:

Yes

15. RELATED IND/NDA/DMF:

Type/Number	Subject	Holder	Status	Review Date	Letter Date
IND 53,731	Synthetic conjugated estrogens Tablet	Duramed Pharm., Inc.	Active	N/A	N/A
			Adequate	see NDA 20-992	N/A
			Adequate	see NDA 20-992	N/A

	Adequate	see NDA 20-992	N/A
	Adequate	see NDA 20-992	N/A
	Adequate	see NDA 20-992	N/A
	Adequate, Reviewed by Dr. D.T. Lin	10/28/99	N/A
	Adequate	see NDA 20-992	N/A
	Adequate, Reviewed by Dr. S. P. Peri	8/3/01	N/A

**16. SUPPLEMENT PROVIDES FOR:**

Addition of a 0.3 mg dosage strength tablet.

**17. SPECIAL PRODUCTS: YES \_\_\_ NO x.**

(If yes, fill out the form for special products and deliver to TIA through team leader for data entry)

**18. COMMENTS**

The chemistry, manufacturing and controls information for the 0.3 mg strength tablet, which is the subject of this efficacy supplement, was reviewed in the original NDA (See Chemistry Reviews #1-#3). However, this dosage strength was withdrawn from the original NDA.

Synthetic conjugated estrogens is a mixture of the sodium sulfate esters of nine estrogens used in the treatment of post menopausal vasomotor symptoms. The original NDA was approved on March 24, 1999 for the 0.625 mg and 0.9 mg strength tablets, with the trademark of Cenestin. Then a 1.25 mg strength tablet was submitted as a supplement (S-006) and approved on March 13, 2000. This Efficacy supplement has been submitted for a 0.3 mg strength tablet manufactured by Duramed in Cincinnati, OH (this dosage strength was submitted to the original NDA but was withdrawn from the NDA before the goal date).

The Division of Biopharmaceutics was consulted for the drug release specification. The drug release specification is the same as in the approved NDA and is satisfactory.

The March 22, 2002 amendment contains updates to the sections of the NDA that have been previously revised due to changes approved in Supplements.

**19. CONCLUSIONS AND RECOMMENDATIONS:**

This Efficacy Supplement for a new dosage strength tablet may be approved pending final acceptable cGMP inspection of all manufacturing facilities cited in this NDA.

**20. REVIEWER NAME**

David T. Lin, Ph.D.  
Chemistry Team Leader

**SIGNATURE**

**DATE COMPLETED**

17-JUN-2002

cc: Original: NDA 20-992/SE1-016

HFD-580/Division File

NDA 20-992/SE1-016

Sponsor: Duramed Pharmaceuticals, Inc.

Drug: Cenestin Tablets  
(synthetic conjugated estrogens, A)

**HFD-580/DSpellLesane**  
**HFD-580/DLin**

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/s/

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David T. Lin  
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CHEMIST  
Awaiting inspection.

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