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*APPLICATION NUMBER:*  
**20-992/S-016**

**CLINICAL PHARMACOLOGY AND  
BIOPHARMACEUTICS REVIEW(S)**

MAR 24 1999

**CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW**

NDA 20-992  
Compound: Synthetic Conjugated Estrogens, A (Cenestin™)  
Sponsor Duramed Pharmaceuticals Inc,  
Type of Submission: New Drug Product  
Date of Submission: December, 8, 1998 (amendment)  
Reviewer: S.W. Johnny Lau, Ameeta Parekh

**Background:** This document provides a further clarification of the Recommendation Section of January 27, 1999 review. A previous review dated March 23, 1999 provided the clarification as follows:

"The Office of Clinical Pharmacology and Biopharmaceutics/Division of Pharmaceutical Evaluation II (OCPB/DPEII) has reviewed the 2 amendments of NDA 20992 dated December 8, 1998 and December 9, 1998. OCPB/DPEII is of the opinion that the sponsor has provided appropriate information to satisfy the bioavailability requirements (21 CFR 320) for the 0.3, 0.625, and 0.9 mg strength Cenestin™ tablets."

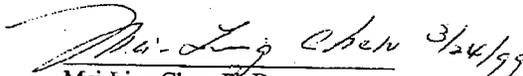
The following statement is a further clarification of the above:

"The Office of Clinical Pharmacology and Biopharmaceutics/Division of Pharmaceutical Evaluation II (OCPB/DPEII) has reviewed the 2 amendments of NDA 20992 dated December 8, 1998 and December 9, 1998. OCPB/DPEII is of the opinion that the sponsor has provided appropriate information to satisfy the bioavailability requirements (21 CFR 320) for

- 1) the 0.625 mg Cenestin™ tablet by providing acceptable in-vivo bioavailability and in-vitro dissolution data, and
- 2) the 0.3 and 0.9 mg Cenestin™ tablets based upon the following conditions, which serve to satisfy the waiver criteria:
  - a) acceptable in vivo bioavailability and in vitro dissolution data on the 0.625 mg tablet
  - b) acceptable comparative in vitro dissolution results between the 0.3, 0.625 and 0.9 mg strength Cenestin™ tablets, and
  - c) acceptable formulation proportionality between the 0.3, 0.625 and 0.9 mg strength Cenestin™ tablets."

  
S.W. Johnny Lau, R.Ph., Ph.D.

  
Ameeta Parekh, Ph.D.

  
Mei-Ling Chen, Ph.D.

cc NDA 20992, HFD 870 (M.Chen, J.Hunt, Parekh, Lau), HFD-580 T. van der Vlugt, D. Moore), CDR (B. Murphy for Drugs)

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/s/

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Venkateswar Jarugula  
10/10/01 01:33:12 PM  
BIOPHARMACEUTICS

Ameeta Parekh  
10/25/01 01:18:48 PM  
BIOPHARMACEUTICS  
I concur

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