

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:NDA20375/S012

CORRESPONDENCE



Food and Drug Administration
Rockville MD 20857

NDA 20-375/S-012

JUN 10 1998

Berlex Laboratories, Inc.
340 Changebridge Road
P.O. Box 1000
Montville, New Jersey 07045-1000

Attention: Geoffrey Millington, Manager

Dear Mr. Millington:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Climara (estradiol transdermal system)
NDA Number: 20-375
Supplement Number: S-012
Date of Supplement: May 27, 1998
Date of Receipt: May 28, 1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on July 27, 1998 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Reproductive and Urologic Drug Products, HFD-580
Office of Drug Evaluation II
Attention: Document Control Room 17B-20
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

Lana L. Pauls, M.P.H.
Chief, Project Management Staff
Division of Reproductive and Urologic
Drug Products, HFD-580
Office of Drug Evaluation II
Center for Drug Evaluation and Research

*Review
G. D. P.
M. D. K.
6-11-98*

NDA 20-375/S-012

Page 2

cc:

Original NDA 20-375/S-012

HFD-580/Div. Files

HFD-580/CSO/D. Moore

SUPPLEMENT ACKNOWLEDGEMENT



ORIGINAL

BERLEX

TELEFAX
UPS OVERNIGHT

May 27, 1998

REVIEWS COMPLETED	
CSO ACTION:	
<input checked="" type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I. <input type="checkbox"/> MEMO
CSO INITIALS	DATE

Drug Development & Technology
Division of Berlex Laboratories, Inc.

340 Changebridge Road
P.O. Box 1000
Montville, NJ 07045-1000
Telephone: (973) 276-2000

Lisa Rarick, M.D., Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation II, HFD-580
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Room 17B-45
Rockville, Maryland 20857-1706

NDA NO. 20-375 REF. NO. 012
NDA SUPPL FOR SLE



Re: **NDA 20-375**
Climara® (estradiol transdermal system)
Supplement- EXPEDITED REVIEW REQUESTED:
Extension of Shelf Life from 24 to 36 Months

*Notice
for
6/12/98*

Dear Dr. Rarick:

Reference is made to our NDA 20-375 for Climara® (estradiol transdermal system) which was approved on December 22, 1994 and was transferred to Berlex Laboratories, Inc. from 3M Pharmaceuticals on November 2, 1995.

Reference is also made to our correspondence of May 15, 1998 wherein we submitted a list of Climara® batches labeled with a 36 month expiration date and not yet distributed for commercial use. Reference is also made to conversations between your representative, Ms. Diane Moore and Ms. June Bray and Ms. Sharon Brown, both of Berlex Laboratories, and Ms. Mary Mathisen of 3M Pharmaceuticals which took place during the period from May 20 to 22, 1998 and within which the issue of the Climara® shelf life was discussed.

In this supplement Berlex Laboratories requests that the Division approve an extension of the shelf life of all 3 approved strengths of Climara® from 24 to 36 months based on 3 year marketed product stability data and FDA SAS Data Analysis. The data and SAS analyses have been submitted by _____ to the Drug Master File on May 27, 1998. A copy of the DMF amendment cover letter is attached.

Climara® (estradiol transdermal system)

May 27, 1998

Page 2

As discussed with Ms. Moore, Berlex has stopped distribution of all product with a 36 month expiration date. We currently do not have an adequate inventory of Climara® with a 24 month expiration date to keep patients supplied with product. In view of this hardship, pursuant to 21 CFR 314.70 (b) Berlex is requesting an expedited review of this supplement.

Please contact the undersigned at (973) 276-2254 if you have any questions concerning this correspondence.

Sincerely,

BERLEX LABORATORIES



Geoffrey P. Millington
Manager
Drug Regulatory Affairs

GPM/letter/clima042

ORIGINAL

BERLEX

TELEFAX
UPS OVERNIGHT

Drug Development & Technology
Division of Berlex Laboratories, Inc.

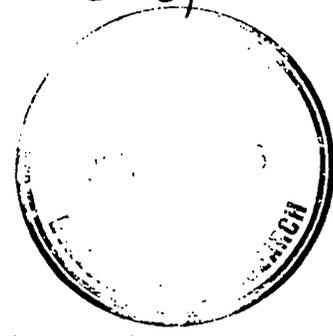
June 3, 1998

NDA SUPP AMEND
SCE-012
BL

340 Changebridge Road
P.O. Box 1000
Montville, NJ 07045-1000
Telephone: (973) 276-2000

Lisa Rarick, M.D., Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation II, HFD-580
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Room 17B-45
Rockville, Maryland 20857-1706

*Noted
6/9/98*
*MAD TL
Out 6-9-98*
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FIL
6/10/98*



Re: NDA 20-375
Climara® (estradiol transdermal system)
GENERAL CORRESPONDENCE

Dear Dr. Rarick:

Reference is made to our NDA 20-375 for Climara® (estradiol transdermal system) which was approved on December 22, 1994 and was transferred to Berlex Laboratories, Inc. from 3M Pharmaceuticals on November 2, 1995.

Reference is also made to conversations between your representative, Ms. Diane Moore and the undersigned which took place on June 2-3, 1998 wherein the issue of the Climara® shelf life and overlabeling was discussed. The primary outcomes of these discussions are as follows:

1) Representatives from Berlex Laboratories and 3M Pharmaceuticals will hold a teleconference with the Division on June 9, 1998 at 10:00 AM to discuss extension of the Climara® shelf-life from 24-36 months based on 36 month stability data which was submitted for review on May 27, 1998.

Attending the teleconference from Berlex:

- Ms. June Bray, Director, DRA
- Ms. Sharon Brown, Associate Director, DRA
- The undersigned

REVIEWS COMPLETED		AP
CSO ACTION:		
<input checked="" type="checkbox"/> LETTER	<input type="checkbox"/> N.A.I.	<input type="checkbox"/> MEMO
Wh		6/11/98
CSO INITIALS		DATE



**TELEFAX
UPS OVERNIGHT**

Drug Development & Technology
Division of Berlex Laboratories, Inc.

June 3, 1998

340 Changebridge Road
P.O. Box 1000
Montville, NJ 07046-1000
Telephone: (973) 276-2000

Lisa Rarick, M.D., Director
Division of Reproductive and Urologic Products
Office of Drug Evaluation II, HFD-580
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Room 17B-45
Rockville, Maryland 20857-1706

**Re: NDA 20-375
Climara® (estradiol transdermal system)
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Attending the teleconference from Berlex:

- Ms. June Bray, Director, DRA
- Ms. Sharon Brown, Associate Director, DRA
- The undersigned

Attending the teleconference from 3M Pharmaceuticals:

- Ms. Mary Mathisen, Senior Regulatory Officer
- Ms. Lisa Schnose, Quality Control

2) Berlex is providing herein samples of labels and cartons which would potentially be used to relabel existing 36-month inventory to 24 months. To adequately overlabel Climara®, corrections must be made in three areas as follows:

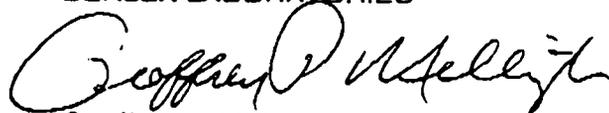
- The primary foil-pouch package. Attachment A contains samples of Climara® foil pouches on which are placed labels (unprinted) which cover the old expiration date and which cannot be removed without damage. These labels could be printed to appear as presented in Attachment B. Please note that the labels used on the pouches in Attachment B are provided only to demonstrate the appearance of the printing; this label stock would not be used to overlabel Climara®.
- The 4-patch system carton. The old packs would be discarded and new packs would be printed and debossed with the 24 month expiration date.
- The 6 x 4 unit packer carton (containing 6 of the 4 system cartons). Attachment C contains samples of 6-patient pack boxes on which have been placed sample labels which would correct the expiration date to 24 months. This label stock destroys the printing underneath if removal is attempted.

Please note that Berlex has determined that the cost of overlabeling the current 36-month dated inventory would be approximately making this process very cost ineffective. In addition, the pouch overlabel appearance is considered undesirable and could potentially be confusing to the consumer. Berlex is very much opposed to overlaying the expiration date on existing inventory, especially in view of the stability data we have submitted which we maintain supports a 36 month expiration date.

Please contact the undersigned at (973) 276-2254 if you have any questions concerning this correspondence.

Sincerely,

BERLEX LABORATORIES



Geoffrey P. Millington
Manager
Drug Regulatory Affairs