

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: April 14, 2005

TO: Daniel Shames, M.D., Director
Division of Reproductive and Urologic Drug Products
HFD-580

VIA: Charlene Williamson, Consumer Safety Officer
Division of Reproductive and Urologic Drug Products
HFD-580

FROM: Jeanine Best, M.S.N., R.N., P.N.P.
Patient Product Information Specialist
Division of Surveillance, Research, and Communication Support
HFD-410

THROUGH: Gerald Dal Pan, M.D., M.H.S., Director
Division of Surveillance, Research, and Communication Support
HFD-410

SUBJECT: DSRCS Review of Patient Labeling for YAZ (drospirenone an ethinyl estradiol) Tablets, NDA 21-873

Background:

The sponsor submitted a Brief Summary Patient Package Insert and a Detailed Patient Package Insert for YAZ (drospirenone an ethinyl estradiol) Tablets, NDA 21-873, on December 22, 2004, as an oral contraceptive and for the treatment of premenstrual dysphoric disorder in women who desire oral contraception.

Comments and recommendations:

We have the following comments and recommendations:

1. Revise the patient labeling for Yaz following the March 2004, Draft Guidance; *Guidance for Industry: Labeling for Combined Oral Contraceptives.*
2. Avoid the use of UPPER CASE lettering to emphasize important information. Upper case lettering is difficult to read. Bold or underline for word or statement emphasis. The tradename is the exception to this recommendation and may be in upper case letters.

Please call us if you have any questions.

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this page is the manifestation of the electronic signature.**

/s/

Jeanine Best
4/14/05 09:55:30 AM
DRUG SAFETY OFFICE REVIEWER

Toni Piazza Hepp
4/14/05 02:45:17 PM
DRUG SAFETY OFFICE REVIEWER
for Gerald Dal Pan



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 21-873

Berlex Laboratories, Inc.
Attention: Nancy Velez, Manager
P.O. Box 1000
Montville, NJ 07045-1000

Dear Ms. Velez:

Please refer to your December 22, 2004 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for YAZ (drospirenone 3mg/ethinyl estradiol 0.02 mg) Tablets.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on February 18, 2005 in accordance with 21 CFR 314.101(a).

In our filing review, we have identified the following potential review issues and have the following information requests:

1. As indicated during the clinical development program, the adequacy of Study 305141 will be a review issue because of the early termination of the study prior to reaching the planned enrollment.
2. Explain the selection of different baselines for different assessment instruments (i.e., why were different times prior to initiation of treatment chosen as baseline?). For example:
 - Daily Record of Severity of Problems Scale (DRSP), the primary endpoint – baseline was average of the DRSP scores from the 2 run-in cycles, Visits 2 and 3.
 - The secondary endpoint instruments (CGI, SF-36, Endicott Q-LES-Q and PMTS) – baseline was Visit 4 (first treatment cycle)
3. Confirm that the cross reference to NDA 21-676 includes not only the original submission, but also all the CMC Amendments to that NDA.
4. Color mock-ups of all carton and container labels should be provided, including any graphics planned for the labeling.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of

deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

If you have any questions, call Charlene Williamson, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Margaret Kober, R.Ph.
Chief, Project Management Staff
Division of Reproductive and Urologic Drug
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Margaret Kober
3/7/05 03:09:22 PM
Chief, Project Management Staff



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-873

Berlex Laboratories, Inc.
Attention: Nancy Velez, Manager
P.O. Box 1000
Montville, NJ 07045-1000

Dear Ms. Velez:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: YAZ™ (drospirenone 3 mg / ethinyl estradiol 0.02 mg) Tablets
Priority Classification: Standard (S)
Date of Application: December 22, 2004
Date of Receipt: December 23, 2004
Our Reference Number: NDA 21-873

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on February 18, 2005 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be October 21, 2005.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. Send all electronic or mixed electronic and paper submission to the Central Document Room at the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room (CDR)
5901-B Ammendale Road
Beltsville, MD 20705-1266

NDA 21-873

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If your submission only contains paper, send it to the following address:

U.S. Postal Service/Courier/Overnight Mail:

Center for Drug Evaluation and Research

Division of Reproductive and Urologic Drug Products

Attention: Division Document Room,

5600 Fishers Lane

Rockville, Maryland 20857

If you have any questions, call Charlene Williamson, Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Margaret Kober, R.Ph.

Chief, Project Management Staff

Division of Reproductive and Urologic drug
Products

Office of Drug Evaluation III

Center for Drug Evaluation and Research

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/s/

Margaret Kober
1/27/05 10:47:30 AM
Chief, Project Management Staff

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVER SHEET

Form Approved: OMB No. 0910-0297
Expiration Date: December 31, 2006.

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: <http://www.fda.gov/cder/pdufa/default.htm>

1. APPLICANT'S NAME AND ADDRESS Berlex, Inc. 340 Changebridge Road (P.O. Box 1000) Montville, NJ 07045-1000	4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER NDA 21-873
2. TELEPHONE NUMBER (Include Area Code) (973) 487 - 2157	5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS 'YES', CHECK THE APPROPRIATE RESPONSE BELOW: <input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION. <input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO: _____ (APPLICATION NO. CONTAINING THE DATA).
3. PRODUCT NAME YAZ™ [Drospirenone 3 mg/Ethinyl Estradiol 0.020 mg] Tablets	6. USER FEE I.D. NUMBER 4892

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE (See Item 7, reverse side before checking box.)
<input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act (See Item 7, reverse side before checking box.)	<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY (Self Explanatory)

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

YES NO

(See Item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services Food and Drug Administration CDER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448	and	Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 Rockville, MD 20852	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.
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SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE <i>Guerra A. Berta</i>	TITLE Manager, Drug Regulatory Affairs	DATE 12/13/2004
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