CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION: NDA 50-751

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CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: NDA 50-751

Trade Name: ATRIDOX

Generic Name:(doxycycline hyclate, 10.0%) in the Atrigel Delivery System for Controlled Release in Subgingival Application

Sponsor: Atrix Laboratories, Inc.

Approval Date: September 3, 1998

Indication: Provides for the use of Atridox for the treatment of chronic adult periodontitis for a gain in clinical attachment, reduction in probing depth, and reduction in bleeding on probing

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 50-751

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 50-751

SEP - 3 1998

Atrix Laboratories, Inc.
Attention: Elaine Gazdeck
2579 Midpoint Drive
Fort Collins, CO 80525

Dear Ms. Gazdeck:

Please refer to your new drug application (NDA) dated March 31, 1997, received April 1, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Atridox™ (doxycycline hyclate, 10.0%) in the Atrigel® Delivery System* for Controlled Release in Subgingival Application *[63.3% N-methyl-2-pyrrolidone and 36.7% poly (DL-lactide)]. We note that this application is subject to the exception provisions of Section 125(d)(2) of Title 1 of the FDA Modernization Act of 1997.

We acknowledge receipt of your submissions dated March 9, April 10 and 24, May 11, and July 2 and 24, 1998. Your submission of July 2, 1998 constituted a full response to our April 7, 1998 action letter. The user fee goal date for this application is January 6, 1999.

This new drug application provides for the use of Atridox for the treatment of chronic adult periodontitis for a gain in clinical attachment, reduction in probing depth, and reduction in bleeding on probing.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed approved labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, immediate container and carton labels). Marketing the product with FPL that is not identical to the enclosed approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavyweight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 50-751." Approval of this submission by FDA is not required before the labeling is used.

In addition, please submit three copies of the introductory promotional material that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional material and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications,
HFD-40
5600 Fishers Lane
Rockville, Maryland 20857

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Please submit one market package of the drug product when available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Roy Blay, Ph.D., Project Manager, at (301) 827-2020.

Sincerely,

/S/

Jonathan K. Wilkin, M.D.
Director
Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

ENCLOSURE

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 50-751

APPROVABLE LETTER

HFD 540/Blay

NDA 50-751

APR 7 1998

Atrix Laboratories, Inc.
Attention: Elaine Gazdeck
2579 Midpoint Drive
Fort Collins, CO 80525

Dear Ms. Gazdeck:

Please refer to your new drug application dated March 31, 1997, received April 1, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ATRIDOX™ (doxycycline hyclate) topical, 8.5%. We note that this application is subject to the exception provisions of Section 125(d)(2) of Title 1 of the FDA Modernization Act of 1997.

We acknowledge receipt of your communications dated April 4 and 16 (2), May 12, 20, and 21, June 6, July 21 and 29, October 23, December 1, 3, 8, 15, and 31, 1997; January 6, 8, and 26, February 13, 18, and 26, and March 2 and 19, 1998.

The User Fee goal date for this application is April 7, 1998.

We have completed the review of this application, including the submitted draft labeling, and it is approvable for the treatment of chronic adult periodontitis for a gain in clinical attachment, reduction in probing depth, and reduction in bleeding on probing. Before this application may be approved, however, it will be necessary for you to submit draft labeling for the drug product identical to the enclosed revised draft labeling. Should additional information relating to the safety or effectiveness of this drug product become available, further revision of the labeling may be required.

Please also update the new drug application with respect to reports of relevant safety information, including all deaths and any adverse events that led to discontinuation of the drug and any information suggesting a substantial difference in the rate of occurrence of common but less serious adverse events. The update should cover all studies and uses of the drug including: (1) those involving indications not being sought in the present submission, (2) other dosage forms, and (3) other dose levels, etc.

In addition, please submit three copies of the introductory promotional material that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional material and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications,
HFD-40
5600 Fishers Lane
Rockville, Maryland 20857

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of such action FDA may take action to withdraw the application.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal or telephone conference with the Division to discuss what further steps need to be taken before the application may be approved.

The drug may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, please contact Roy Blay, Ph.D., at (301) 827-2020.

Sincerely yours,

/S/ 4/7/98

Jonathan K. Wilkin, M.D.
Director
Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

ENCLOSURE

cc:
Original NDA 50-751
HFD-540/Division File
HFD-105/Weintraub (with draft labeling)
HFD-002/Lumpkin (with draft labeling)
HFD-95 DDM-DIAB (with draft labeling)
HFD-222
HFD-101/L.Carter (with draft labeling)
District Office (with draft labeling)
HFD-830/ONDC Division Director (with draft labeling)
HF-2/Medwatch (with draft labeling)
HFD-40/DDMAC(with draft labeling)
HFD-613/OGD (with draft labeling)
HFD-540/MO/Kelsey(with draft labeling)
HFD-540/MO/Hyman (with draft labeling)
HFD-540/CHEM/Pappas (with draft labeling)
HFD-540/CHEM/DeCamp (with draft labeling)
HFD-520/MICRO/Marsik (with draft labeling)
HFD-520/MICRO/Sheldon (with draft labeling)
HFD-540/PHARM/Jacobs (with draft labeling)
HFD-540/PHARM/See (with draft labeling)
HFD-160/MICRO/Uratani (with draft labeling)
HFD-160/MICRO/Cooney (with draft labeling)
HFD-725/BIOSTAT/Srinivasan (with draft labeling)
HFD-725/BIOSTAT/Gao (with draft labeling)
HFD-880/BIOPHARM/Bashaw (with draft labeling)
HFD-880/BIOPHARM/Wang (with draft labeling)
HFD-540/SUPV PROJ MGR/Kozma-Fornaro (with draft labeling)
HFD-540/PROJ MGR/Blay (with draft labeling)
Concurrences:
HFD-540/CHEM/Pappas 4.2.98
HFD-540/PHARM/Jacobs 4.2.98
HFD-540/PHARM/See 4.1.98
HFD-725/BIOSTAT/Srinivasan 4.1.98
HFD-725/BIOSTAT/Gao 4.1.98
HFD-880/BIOPHARM/Bashaw 4.3.98
HFD-540/MO/Kelsey 4.7.98
HFD-540/SUPV PROJ MGR/Kozma-Fornaro 4.7.98
Drafted by: rab/April 7, 1998/c:\royblay\letters\nda\approval\50751.003. The label version is c:\royblay\letters\nda\labeling\50751.004

APPROVABLE (AE)