CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number: NDA 20535

Trade Name: DURACT

Generic Name: BROMFENAC SODIUM

Sponsor: WYETH-AYERST LBORATORIES

Approval Date: JULY 13, 1997

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APPLICATION: NDA 20535

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Chemistry Review(s)	X			
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Pharmacology Review(s)	X			
Statistical Review(s)	X			
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CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 20535

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-535

JUL 15 1997

Wyeth-Ayerst Laboratories
Attention: Joseph N. Bathish
Senior Vice President: Worldwide Regulatory Affairs
145 King of Prussia Road C-2
Radnor, Pennsylvania 19087

Dear Mr. Bathish:

Please refer to your December 31, 1994, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Duract (bromfenac sodium capsules) 25 mg. Please also refer to our letters dated December 28, 1995, September 30, 1996, and May 22, 1997.

We acknowledge your correspondence and submissions dated September 30, October 3, 18, and 22, November 13 and 26, and December 23, 1996; and January 16, February 24, March 3 and 31, April 3 and 25, and May 7 and 12, and June 30, 1997.

We have completed the review of this application including the submitted draft labeling 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 May 12, 1997, submission. Accordingly, this application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the May 12, 1997, draft labeling. Marketing the product with FPL that is not identical to this draft labeling may render the product misbranded and unapproved.

Please submit sixteen 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 heavy weight paper or similar material. For administrative purposes this submission should be designated "FINAL PRINTED LABELING" for approved NDA 20-535. Please also submit sixteen copies of container and carton labels for this product. Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of that labeling may be required.

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 send one copy to the Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products, and two copies of both the promotional material and the package inserts directly to:

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

Please note that any advertising and/or promotional activities of this product will be considered false and misleading under Section 502 of the Act if it presents suggestions or representations that this product is safe and effective for any use longer than 10 days or for any indication other than short-term management of pain. This guidance constitutes notice of activities that may be considered to be violations of the Act. Failure to comply with this guidance may result in regulatory action without further notice.

If you have any questions, please contact Chin Koerner, M.S., Project Manager, at (301) 827-2090.

Sincerely,

MWeintraub 7/15/97

Michael Weintraub, M.D.
Office Director
Office of Drug Evaluation V
Center for Drug Evaluation and Research

cc:
NDA 20-535
HFD-550/Div Files
HF-2/ Med Watch (with draft/ final labeling)
HFD-002/ ORM (with draft/ final labeling)
HFD-92 (with draft/ final labeling)
HFD-105
HFD-550/Chambers
HFD-550/Medical /Widmark/Hyde JEH 7-14-97
HFD-550/Pharmacology/Yang/Chen XY 7-14-97 AWC 7-14-97
HFD-830/Chemistry/Ho/Patel
HFD-550/Statistics/Stein/Leung 7-14-97 MDP 7-15-97
HFD-880/Pharmacokinetics/Bashaw 7/14/97
HFD-550/ Project Managers/Koerner/Lobianco 7/14/97
HFD-830/Chen
HFD-40/ DDMAC (with draft/ final labeling)
HFD-613/ OGD (with draft/ final labeling)
HFD 735/DPE (with draft/ final labeling)
HFD-20/ Press Office (with draft/ final labeling)
District office
HFD-101/Carter
HFD-205

drafted by: cck/July 10, 1997
initialed by:
final:

APPROVAL (AP)
saved as ap7.710

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20535

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-535

SEP 20 1996

Wyeth-Ayerst Laboratories
Attention: Joseph N. Bathish
Senior Vice President: Worldwide Regulatory Affairs
145 King of Prussia Road C-2
Radnor, Pennsylvania 19087

Dear Mr. Bathish:

Please refer to your December 29, 1994, new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for bromfenac sodium oral capsules. Reference is also made to our approvable letter dated December 28, 1995.

We acknowledge your correspondence and amendments dated February 10, March 24 and 27, April 18 and 24, May 10 and 31, June 6, 9, and 30, July 26 (two), August 10, 11, 14, 24, and 30, September 8, 13, 15, 19, and 26, October 20 and 30, November 1, 7, 14, 16, and 22 (two), and December 11 (two) and 18, 1995, January 4 and 10 (two), February 14, 28, and 29, April 3 (two), 12, and 19, May 3, and July 11 and 19, 1996.

We have completed the review of this application and it is approvable. Before this application may be approved, however, it will be necessary for you to submit revised labeling identical to the enclosed draft labeling. Please submit revised carton and package labeling that is consistent with the enclosed draft labeling. Should additional information relating to the safety and effectiveness of the drug become available, revision of that labeling may be required.

We agree to meet at your request on November 4, 1996, to discuss your concerns related to the hepatic effects, and the two week treatment duration.

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:

Division of Drug Marketing, Advertising and Communications, HFD-40
FDA
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.

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

Should you have any questions, please contact:

Chin Koerner
Project Manager
Telephone: (301) 827-2090

Sincerely,

Michael Weintraub

Michael Weintraub, M.D.
Office Director
Office of Drug Evaluation V
Center for Drug Evaluation and Research

enclosure: draft labeling

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

NDA 20-535

Food and Drug Administration
Rockville MD 20857

Wyeth-Ayerst Laboratories
145 King of Prussia Road C-2
Radnor, Pennsylvania 19087

DEC 28 1995

Attention: Joseph N. Bathish
Senior Vice President, Worldwide Regulatory Affairs

Dear Mr. Bathish:

Please refer to your December 29, 1994, new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for bromfenac sodium 25 mg and 50 mg oral capsules.

We acknowledge receipt of your amendments dated June 6, August 14, September 13, and November 22, 1995.

We have completed the review of this application as submitted with draft labeling. Before the application may be approved it will be necessary for you to submit the following information:

1. Satisfactory resolution of any outstanding Environmental Assessment deficiencies transmitted to your company by facsimile on December 19, 1995.

2. Satisfactory resolution of outstanding Chemistry issues. These include recommendations transmitted to your company by facsimile on December 15, 1995, and approval of a tradename for bromfenac sodium.

3. A satisfactory final printed label to reflect:
   - Short term usage (up to 2 weeks) for management of pain.
   - Removal of any references for treatment of chronic pain including but not limited to treatment of osteoarthritis and rheumatoid arthritis.
   - Appropriate warnings and precautions for hepatic effects.
   - Removal of any references for treatment of dysmenorrhea.
   - A decrease in the maximum recommended daily dose to 150 mg.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of that FPL may be required.

Please submit sixteen copies of the printed labels and other labeling, ten of which are individually mounted on heavy weight paper or similar material.

Under 21 CFR 314.50(d)(5)(vi)(b), we request that you update your NDA by submitting all safety information you now have regarding your new drug. Please submit updated information as listed below:

1. A retabulation of all safety data including results of trials that were still ongoing at the time of NDA submission. The tabulation can take the same form as your initial submission. Tables comparing adverse reactions at the time the NDA was submitted to current adverse reaction data will facilitate review.

2. A retabulation of drop-outs and identify drop-puts. These provide discussion as necessary.

3. Submission of details of significant changes or findings, if any.

4. A summary of the worldwide experience on the safety of this drug.

5. Submission of case report forms for each patient who died during a clinical study or who did not complete a study because of an adverse event.

Please 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 send one copy to the Division of Anti-Inflammatory, Analgesic, and Dental Drug Products and two copies of both the promotional material and the package inserts directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising and Communications, HFD-240
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.

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

Should you have any questions, please contact:

Chin Koerner
Project Manager
Telephone: (301) 827-2090

Sincerely yours,

Review Team
Division of Anti-Inflammatory, Analgesic,
and Dental Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Michael Weintraub, M.D.
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Chemist

Josie Yang, Ph.D.
Pharmacologist

E. Dennis Bashaw, Pharm.D.
Pharmacokineticist

Richard Stein, Ph.D.
Statistician

Chin Koerner, M.S.
Project Manager

cc:
Original NDA 20-535
HFD-550/Div. Files
HFD-2/MLumpkin
HFD-80
HFD-100
HFD-105/MWeintraub
HFD-550/CKoerner
DISTRICT OFFICE
HFD-240/SSherman (with draft labeling)
HFD-613 (with draft labeling)
HFD-735/CBarash (with draft labeling)

drafted: CKoerner/12- 11-95
R/D Int. by:JHyde, RWidmark, SSchmidt 12-19-95
F/T by:SLewis-12/22/95/MMatheny-12/26/95
saved as 20535lt5.@20

APPROVABLE (AE)