

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20939

CORRESPONDENCE



DEPARTMENT OF HEALTH & HUMAN SERVICES

D. Roeder

Food and Drug Administration
Rockville MD 20857

NDA 20-939

MAY 11 1999

Biovail Laboratories Incorporated
c/o Keller and Heckman
Attention: John B Dubeck
1001 G Street, N.W.
Washington, D.C. 20001

Dear Mr. Dubeck:

Please refer to your November 5, 1997 new drug application (NDA) and to the February 10, 1999 informal conference between your representatives and FDA staff concerning our refusal to file your application. This also refers to your April 15, 1999 request that the application be filed over protest.

In response to your request, and in accordance with 21 CFR 314.101(c), the application will be filed over protest. It is the policy of the Agency that the filing of an application over protest will be regarded by the Agency as submission of a new original application for user fee purposes (see Interim Guidance on Applicability of User Fees to (1) Applications Withdrawn Before Filing, or (2) Applications the Agency Has Refused to File and That Are Resubmitted or Filed Over Protest, July 12, 1993). Therefore, the fees applicable to a new submission must be submitted to the Agency.

Please note that the user fee review clock started on the day of the informal conference, February 10, 1999.

If you have any questions, please contact:

Mr. David Roeder
Regulatory Health Project Manager
(301) 594-5313

Sincerely,

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research



D. Rueda

Food and Drug Administration
Rockville MD 20857

NDA 20-939

MAR 27 1998

Biovail Corporation International
Attention: Ms. Mimi Brennan
2488 Dunwin Drive
Mississauga, Ontario
Canada L5L 1J9

Dear Ms. Brennan:

Please refer to your November 5, 1997 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for diltiazem hydrochloride extended-release capsules, 120, 180, 240 and 300 mg. We note that this application could not be considered for filing until we received the user fee payment on November 20, 1997. Please also refer to our letter to you of January 13, 1998. This letter supersedes our correspondence of January 13, 1998 and should be considered as effective on January 13, 1998.

We have given your NDA a preliminary review, and we find it is not sufficiently complete to merit a critical medical and technical review. Thus, it will not be filed as a new drug application within the meaning of section 505(b) of the Act.

We are refusing to file this NDA under 21 CFR 314.101(d) for the following reason:

NDA 20-939 contains no nonclinical pharmacology or toxicology data. It is your intent to rely on the right of reference for those data that was granted to you by Hoechst Marion Roussel (HMR) to support the approval of your NDA 20-401. As we had informed you in our letter dated November 8, 1996 (enclosed), the right of reference that was granted to you by HMR for NDA 20-401 does not permit reference to HMR's NDA 18-602 for any once-daily diltiazem product that was not originally submitted to NDA 20-401. The diltiazem product covered by NDA 20-939 is different from the product covered by NDA 20-401. We therefore consider NDA 20-939 to be incomplete and can not be filed according to 21 CFR 314.101(d)(3).

Within 30 days of the date of this letter, you may request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusions, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3). If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(3). The filing date will be 60 days after the date you requested the informal conference.

Under the Food and Drug Administration Modernization Act of 1997, FDA will retain one-quarter of the full application fee and refund the remainder to you. If you decide to file the application over protest, the filing of the application over protest will be regarded by the Agency as a new original application for user fee purposes, and will be assessed a user fee applicable to a new submission.

If you have any questions please call:

Mr. David Roeder
Regulatory Health Project Manager
(301) 594-5313

Sincerely yours,

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

cc:

Orig. NDA
HFD-110
HFD-002/ORM
HFD-92/DDM-DIAB
DISTRICT OFFICE
HFD-810/ONDC Division Director
GCF-1/LDickinson
HFD-110/DRoeder
sb/3/27/98

~~REFUSAL TO FILE (RF)~~

General Correspondence



Food and Drug Administration
Rockville MD 20857

NDA 20-939

MAR 27 1998

Biovail Corporation International
Attention: Ms. Mimi Brennan
2488 Dunwin Drive
Mississauga, Ontario
Canada L5L 1J9

Dear Ms. Brennan:

Please refer to your November 5, 1997 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for diltiazem hydrochloride extended-release capsules, 120, 180, 240 and 300 mg. We note that this application could not be considered for filing until we received the user fee payment on November 20, 1997. Please also refer to our letter to you of January 13, 1998. This letter supersedes our correspondence of January 13, 1998 and should be considered as effective on January 13, 1998.

We have given your NDA a preliminary review, and we find it is not sufficiently complete to merit a critical medical and technical review. Thus, it will not be filed as a new drug application within the meaning of section 505(b) of the Act.

We are refusing to file this NDA under 21 CFR 314.101(d) for the following reason:

NDA 20-939 contains no nonclinical pharmacology or toxicology data. It is your intent to rely on the right of reference for those data that was granted to you by Hoechst Marion Roussel (HMR) to support the approval of your NDA 20-401. As we had informed you in our letter dated November 8, 1996 (enclosed), the right of reference that was granted to you by HMR for NDA 20-401 does not permit reference to HMR's NDA 18-602 for any once-daily diltiazem product that was not originally submitted to NDA 20-401. The diltiazem product covered by NDA 20-939 is different from the product covered by NDA 20-401. We therefore consider NDA 20-939 to be incomplete and can not be filed according to 21 CFR 314.101(d)(3).

Within 30 days of the date of this letter, you may request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusions, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3). If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(3). The filing date will be 60 days after the date you requested the informal conference.

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If you have any questions please call:

Mr. David Roeder
Regulatory Health Project Manager
(301) 594-5313

Sincerely yours,

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

cc:

Orig. NDA

HFD-110

HFD-002/ORM

HFD-92/DDM-DIAB

DISTRICT OFFICE

HFD-810/ONDC Division Director

GCF-1/LDickinson

HFD-110/DRoeder

sb/3/27/98

REFUSAL TO FILE (RF)



NDA 20-939

JAN 13 1998

Biovail Corporation International
Attention: Ms. Mimi Brennan
2488 Dunwin Drive
Mississauga, Ontario
Canada L5L 1J9

Dear Ms. Brennan:

Please refer to your November 5, 1997 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for diltiazem hydrochloride extended-release capsules, 120, 180, 240 and 300 mg. We note that this application could not be considered for filing until we received the user fee payment on November 20, 1997.

We have given your NDA a preliminary review, and we find it is not sufficiently complete to merit a critical medical and technical review. Thus, it will not be filed as a new drug application within the meaning of section 505(b) of the Act.

We are refusing to file this NDA under 21 CFR 314.101(d) for the following reasons:

1. NDA 20-939 contains no nonclinical pharmacology or toxicology data. It is your intent to rely on the right of reference for those data that was granted to you by Hoechst Marion Roussel (HMR) to support the approval of your NDA 20-401. As we had informed you in our letter dated November 8, 1996 (enclosed), the right of reference that was granted to you by HMR for NDA 20-401 does not permit reference to HMR's NDA 18-602 for any once-daily diltiazem product that was not originally submitted to NDA 20-401. The diltiazem product covered by NDA 20-939 is different from the product covered by NDA 20-401. We therefore consider NDA 20-939 to be incomplete and can not be filed according to 21 CFR 314.101(d)(3).
2. Biovail Laboratories Incorporated is the applicant for NDA 20-939 as well as a pending application (ANDA 75-116) with the Office of Generic Drugs. We consider it an inappropriate use of the Agency's resources to review the same product under two different applications from the same applicant. Therefore, according to 21 CFR 314.101(d)(8), NDA 20-939 should not be filed.

Within 30 days of the date of this letter, you may request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusions, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3). If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(3). The filing date will be 60 days after the date you requested the informal conference.

Under the Food and Drug Administration Modernization Act of 1997, FDA will retain one-quarter of the full application fee and refund the remainder to you. If you decide to file the application over protest, the filing of the application over protest will be regarded by the Agency as a new original application for user fee purposes, and will be assessed a user fee applicable to a new submission.

If you have any questions please call:

Mr. David Roeder
Regulatory Health Project Manager
(301) 594-5313

Sincerely yours,

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

cc:

Orig. NDA

HFD-110

HFD-002/ORM

HFD-92/DDM-DIAB

DISTRICT OFFICE

HFD-810/ONDC, Division Director

HFD-110/DRoeder

sb/12/30/97;1712/98

R/D: NMorgenstern/1/12/98

REFUSAL TO FILE (RF)



Roeder

Food and Drug Administration
Rockville MD 20857

NDA 20-939

DEC 31 1997

Biovail Corporation International
Attention: Mr. George E. Markus
2488 Dunwin Drive
Mississauga, Ontario
Canada L5L 1J9

Dear Mr. Markus:

We acknowledge receipt of your November 17, 1997 correspondence notifying the Food and Drug Administration of the change of ownership of the following new drug application (NDA):

Name of Drug: Diltiazem HCl Extended Release Capsules, 180, 240 and 300 mg

NDA Number: 20-939

Date of Submission: November 17, 1997

Date of Receipt: November 20, 1997

Name of New Owner: Biovail Laboratories Incorporated

Name of Previous Owner: Biovail Corporation International

You are responsible for any correspondence outstanding as of the effective date of the transfer.

If you have any questions, please contact:

Mr. David Roeder
Regulatory Health Project Manager
(301) 594-5313

Sincerely yours,

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research



Reeder

Food and Drug Administration
Rockville MD 20857

NDA 20-939

Biovail Corporation International
Attention: Ms. Mimi Brennan
2488 Dunwin Drive
Mississauga, Ontario
Canada L5L 1J9

Dear Ms. Brennan:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug and Cosmetic Act for diltiazem hydrochloride extended-release capsules.

You were notified in our letter dated November 13, 1997 that your application for diltiazem hydrochloride extended-release capsules was not accepted for filing due to non-payment of fees required under the Prescription Drug User Fee Act of 1992.

This is to notify you that the Agency has received all fees owed and your application have been accepted as of November 20, 1997.

Unless we notify you within 60 days of the above date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on January 19, 1998 in accordance with 21 CFR 314.101(a).

Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

Sincerely yours,

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: John B. Dubeck
1001 G Street, N.W.
Washington, D.C. 20001



DEPARTMENT OF HEALTH & HUMAN SERVICES

D. Roeder
Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-939

NOV 13 1997

Biovail Corporation International
Attention: Ms. Mimi Brennan
2488 Dunwin Drive
Mississauga, Ontario
Canada L5L 1J9

Dear Ms. Brennan:

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: Diltiazem HCl Extended-Release Capsules

Therapeutic Classification: S

Date of Application: November 5, 1997

Date of Receipt: November 7, 1997

Our Reference Number: NDA 20-939

We have not received the appropriate user fee for this application. Under section 736(e) of the Prescription Drug User Fee Act of 1992 (PDUFA), an application is considered incomplete and will not be accepted for filing until all fees owed have been paid. Therefore, this application is not accepted for filing. We will not begin a review of this application's adequacy for filing until FDA has been notified that the appropriate fee has been paid. Payment should be submitted to the following address:

Food and Drug Administration
P.O. Box 360909
Pittsburgh, PA 15251-6909

If checks are to be sent by a courier that requires a street address, they can be forwarded to the following address:

NOTE: This address is for courier delivery only. Make sure the FDA Post Office Box Number (P.O. Box 360909) is on the enclosed check.

The receipt date for this submission (which begins the review for filability) will be the date the review division is notified that payment was received by the bank.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

Sincerely yours,

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: John B. Dubeck
1001 G Street, N.W.
Washington, D.C. 20001

cc
Original NDA
HFD-110
HFD-110/DRoeder
sb/11/13/97

UNACCEPTABLE FOR FILING (UN)