CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:NDA 20850

CORRESPONDENCE

NDA 20-850

SEP - 1 1998

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Ms. Heidi C. Reidies
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877

Dear Ms. Reidies:

Please refer to your new drug application for Micardis (telmisartan) Tablets

In reviewing your submission of September 26, 1997, our Division Director, Medical Group Leader, Statistician and Pharmacologist have comments and recommendations. Our concerns with your submission are detailed as part of this correspondence.

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

Enclosures
R Lipicky memo 8/25/98
A Karkowsky memo 8/13/98
W Nuri 8/4/98
W Nuri 8/18/98
G Jagadeesh 8/18/98

cc:
Original
~~HFD-110~~
~~HFD-110/KBongiovanni~~
sb/9/1/98

GENERAL CORRESPONDENCE

AUG 17 1998

NDA 20-850

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Ms. Heidi C. Reidies
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877

Dear Ms. Reidies:

Please refer to your new drug application for Micardis (telmisartan) Tablets

In reviewing your submission of September 26, 1997, our Medical Officer, Statistician and Biopharmaceutist have comments and recommendations. Our concerns with your submission are detailed as part of this correspondence

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

Enclosures
KU MOR 8/3/98
EFadiran Biopharm Review 8/7/98
WNuri Stat Review 6/19/98

cc:
Original
HFD-110
HFD-110/KBongiovanni
sb/8/14/98;8/17/98
R/D: NMorgenstern/8/14/98

GENERAL CORRESPONDENCE

K. Borgstrom

JUL - 9 1998

NDA 20-850

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Ms. Heidi Reidies
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877

Dear Ms. Reidies:

Please refer to your pending September 26, 1997 new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Micardis (telmisartan) 40 and 80 mg Tablets.

We also refer to your submissions dated May 15 and June 8, 1998.

We have completed our review of the chemistry, manufacturing and controls section of your May 15 and June 8, 1998 submissions and have the following comments and information requests:

1. On the carton label, we now recommend:

   Important: Moisture sensitive tablets - do not remove from blisters until just before administration.

2. In addition, we recommend that the carton label state that:

   Each tablet contains 40 mg of telmisartan.

or:

Each tablet contains 80 mg of telmisartan.

in addition to 40 mg (or 80 mg) and the 40 or 80 icon.

3. We recommend for the back of the blister pack:

REMOVE FROM BLISTER AT TIME OF USE

instead of the DISPENSE phrase. Repetition is not necessary if space is limited.

4. The day of week reminder would be more useful if it appeared only at each tablet position.

We would appreciate your prompt written response so we can continue our evaluation of your NDA.

These comments are being provided to you prior to completion of our review of the application to give you preliminary notice of issues that have been identified. Per the user fee reauthorization agreements, these comments have been reviewed only to the level of the discipline team leader. They do not reflect division director input or concurrence and should not be construed to do so. These comments are subject to change as the review of your application is finalized. In addition, we may identify other information that must be provided prior to approval of this application.

If you respond in the current review cycle we may or may not consider your response prior to taking an action on your application. In the meantime, we are continuing our review of your application.

If you have any questions, please contact:

Ms. Kathleen Bongiovanni
Regulatory Health Project Manager
(301) 594-5334

Sincerely yours,

Kasturi Srinivasachar, Ph.D.
Chemistry Team Leader, DNDC I
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Archival NDA 20-850
HFD-110/Div. Files
HFD-810/DNDC I Division Director (only for CMC related issues)
DISTRICT OFFICE
HFD-110/K.Bongiovanni
HFD-110/C.Beminger
sb/6/30/98
cg/7/09/98
Initialed by:
filename: n20850ir#1.wpd

INFORMATION REQUEST (IR)

DEPARTMENT OF HEALTH & HUMAN SERVICES

K. Borgovanni

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-850

MAY 26 1998

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Ms. Heidi Reidies
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877

Dear Ms. Reidies:

Please refer to your pending September 26, 1997 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug and Cosmetic Act for Micardis (telmisartan) 40 and 80 mg Tablets.

We also refer to your amendment dated October 28, 1997.

We have completed our review of the chemistry, manufacturing, and controls section of your submissions and have identified the following deficiencies:

1. The sampling plan for finished pharmaceuticals, as described in volume 1.006, page 68, is not sufficient to prevent product labeling errors. Please institute a more thorough plan and provide it to us in a prompt manner, so that we may continue with our review.

2. We note that a telmisartan tablet reprocessing procedure is not provided in NDA 20-850 as submitted. We request that you either submit a tablet reprocessing procedure as an amendment or commit to submitting a supplement if you develop such a procedure.

3. We will establish dissolution specifications for Micardis (telmisartan) based on statistical analysis of your individual tablet dissolution data and we will convey comments, if any, about dissolution specifications after we complete the Biopharmaceutics part of your submission.

4. Please consider using the following storage statement in the package insert:

5. You may use one of the following abbreviated storage statements if space on the immediate container is limited. In this case, the full statement, as above, must appear on the outer carton and in the package insert.

or

6. Please certify that the used to make the magnesium stearate is from a Bovine Spongiform Encephalopathy (BSE)-free country.

7. For drug substance batch size, the submission states that "Multiples or submultiples of the mentioned quantities are . . . possible" (quoted from volume 1.003, page 50). Please submit the batch sizes that have been validated by experience.

We would appreciate your prompt written response so we can continue our evaluation of your NDA.

If you have any questions, please contact:

Ms. Kathleen Bongiovanni
Regulatory Health Project Manager
(301) 594-5334

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

cc:
Original NDA
HFD-110
HFD-810/CHoiberg
HFD-110/CBerninger
HFD-110/KBongiovanni
sb/5/8/98;5/15/98
R/D: CBerninger/5/11/98
JShort/5/11/98
NMorgenstern/5/13/98

INFORMATION REQUEST (IR)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-850

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Ms. Heidi C. Reidies
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877

OCT 2 - 1997

Dear Ms. Reidies:

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: Telmisartan 40 and 80 mg Tablets

Therapeutic Classification: S

Date of Application: September 26, 1997

Date of Receipt: September 26, 1997

Our Reference Number: NDA 20-850

Unless we notify you within 60 days of our receipt 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 November 25, 1997 in accordance with 21 CFR 314.101(a).

Under 21 CFR 314.102(c) of the new drug regulations you may request an informal conference with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the application's ultimate approvability. Alternatively, you may choose to receive such a report by telephone. Should you wish a conference, a telephone report, or if you have any questions concerning this NDA, please contact:

Ms. Kathleen Bongiovanni
Regulatory Health Project Manager
(301) 594-5334

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
Original NDA
HFD-110
HFD-110/KBongiovanni
sb/9/30/97;10/17/97

ACKNOWLEDGMENT (AC)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

IND

APR 29 1997

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Ms. Heidi Reidies
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877

Dear Ms. Reidies:

Please refer to your investigational new drug application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for telmisartan.

We also refer to your amendments dated March 7 and 28, 1997, serial numbers 095 and 099.

We have completed the review of your submissions, and we concur with your designation of the starting materials used in the synthesis of telmisartan drug substance as described in the above amendments.

If you have any questions, please contact:

Ms. Kathleen Bongiovanni
Regulatory Health Project Manager
(301) 594-5334

Sincerely yours,

/S/

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

Bongiovanni

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

IND

JAN 22 1997

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Ms. Heidi C. Reidies
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877

Dear Ms. Reidies:

Please refer to your investigational new drug application submitted pursuant to section 505(i) of the Federal Food, Drug and Cosmetic Act for telmisartan.

Reference is also made to your letter dated December 13, 1996, serial number 085, requesting a waiver of the requirements for the submission of paper case report tabulations in conjunction with the forthcoming telmisartan new drug application.

You have represented in your letter that the electronic case report tabulations have been prepared in a manner that is substantially consistent with the FDA's proposed rules regarding electronic signatures and electronic records, proposed 21 CFR Part 11, 59 FR 45160 (August 31, 1994).

We have concluded that under 21 CFR 314.90(b)(2), your alternative electronic submission justifies a wavier of the "hard copy" requirements of 21 CFR 314.50(f). Consequently, your waiver request is granted.

Should future retrieval be deemed necessary, and as condition of granting this waiver, you are required to maintain paper copies of the case report forms and tabulations as required under 21 CFR 312.57(b).

If you have any further questions, please contact:

Ms. Kathleen Bongiovanni
Regulatory Health Project Manager
(301) 594-5334

Sincerely yours,

Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research

cc
Orig.
HFD-1
HFD-070/DMoss
HFD-110
HFD-110/KBongiovanni
sb/12/26/96;1/2/97
R/D: NMorgenstern/12/30/96

ACKNOWLEDGEMENT