CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 21-162

CORRESPONDENCE

ORIGINAL

Boehringer Ingelheim

Raymond Lipicky, M.D., Director
Division of Cardio-Renal Drug Products, HFD-110
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
5600 Fishers Lane
Rockville, MD 20852

Boehringer Ingelheim
Pharmaceuticals, Inc.

April 26, 2000

(SW)

Telmisartan/Hydrochlorothiazide Combination Tablets
NDA 21-162

AMENDMENT #2 TO A PENDING APPLICATION

Clinical

Heidi C. Reidies
Senior Associate Director
Drug Regulatory Affairs
Telephone (203) 798-4345
Telefax (203) 791-6262
E-Mail hreidies@rdg.boehringer-ingelheim.com

900 Ridgebury Rd/P.O. Box 368
Ridgefield, CT 06877-0368
Telephone (203) 798-9988

Dear Dr. Lipicky:

Pursuant to 21 CFR 314.50(d)(5)(vi)(b), Boehringer Ingelheim Pharmaceuticals, Inc. is amending the above referenced NDA to provide updated safety information for telmisartan/hydrochlorothiazide combination tablets.

Please find the following report:
Pound J. *Four Month Safety Update Report for NDA 21-162, Telmisartan/Hydrochlorothiazide Combination Tablets*. Unpublished Report U00-3108 (April 12, 2000).

This safety report is an update of the Integrated Summary of Safety (ISS) provided in the original NDA, submitted December 29, 1999. It concludes that the updated safety profile of telmisartan and hydrochlorothiazide administered in combination is consistent with that reported in the ISS in the original NDA.

All appendices to the safety update report are being provided with this submission, except Appendix 3, which contains case report forms for patients who died or discontinued due to adverse events (report volumes 5-13); these will be provided upon request.

During a telephone conversation on April 25, 2000, Mr. E. Fromm advised that BI need not plan to prepare an additional safety update report for telmisartan/hydrochlorothiazide tablets for submission prior to NDA approval. If, after review of this report, for example, it is decided that a second safety update report is required, we request to be informed as soon as possible, to accommodate the lead time that is required to prepare it.

ORIGINAL

Boehringer Ingelheim

Please contact me if you have any questions regarding this submission.

Sincerely,

Heidi C. Reidies
Drug Regulatory Affairs

Copy: Mr. E. Fromm
Reviewer copy: Dr. A. Karkowski

Safety Review

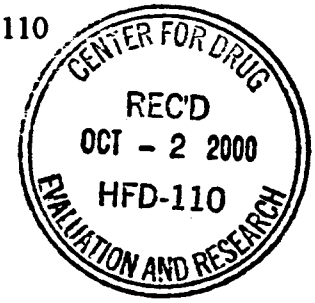
Boehringer Ingelheim submitted, on April 26, 2000, four volumes of safety update reports. These are too voluminous to be included with this package but are available in the Division Document room.

Dr. Karkowsky's review of the safety reports is included in his Medical review.

APPEARS THIS WAY
ON ORIGINAL

Boehringer Ingelheim

Raymond Lipicky, M.D., Director
Division of Cardio-Renal Drug Products, HFD-110
Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room
5600 Fishers Lane
Rockville, MD 20852



Boehringer Ingelheim
Pharmaceuticals, Inc.

September 29, 2000

Telmisartan/Hydrochlorothiazide Combination Tablets
NDA 21-162

AMENDMENT #19 TO A PENDING APPLICATION
Human Pharmacokinetics and Bioavailability

Heidi C. Reidies
Senior Associate Director
Drug Regulatory Affairs

Telephone (203) 798-4345
Telefax (203) 791-6262
E-Mail hreidies@rdg.boehringer-ingelheim.com

900 Ridgebury Rd/P.O. Box 368
Ridgefield, CT 06877-0368
Telephone (203) 798-9988

Dear Dr. Lipicky:

Reference is made to the telefax sent September 15, 2000, informing us of the recommendation from the Office of Clinical Pharmacology and Biopharmaceutics to change the dissolution specification for telmisartan/hydrochlorothiazide tablets to Q= [redacted] at [redacted] minutes for each of the tablet components, telmisartan and hydrochlorothiazide.

We hereby accept this FDA recommendation. The revised testing specifications for telmisartan/hydrochlorothiazide tablets will reflect these limits.

Reference is also made to a telephone discussion on September 27, 2000, with Dr. P. Marroum and Dr. A. Dorantes, during which Dr. P. Cafiero pointed out that Boehringer Ingelheim has limited batch experience with telmisartan/hydrochlorothiazide tablets. In response, Dr. Marroum stated that FDA would be willing to reconsider the dissolution specifications on an expedited basis, if data from production batches warranted such action. We appreciate this offer, and will keep it in mind.

Please incorporate this information into NDA 21-162.

Sincerely,

Heidi C. Reidies
Drug Regulatory Affairs

Desk copies: Mr. E. Fromm