CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:NDA 19-778/S-028

CHEMISTRY REVIEW(S)

OCT 27 1997

CHEMIST'S REVIEW	1. ORGANIZATION HFD-110	2. NDA Number 19-778
3. Name and Address of Applicant (City & State) Merck Research Laboratories West Point, PA 19486		4. Supplement(s) Number(s) Date(s) S-028 20 Oct 97
5. Drug Name Prinzide	6. Nonproprietary Name Lisinopril/HCTZ	7. Amendments & Other (reports, etc) - Dates
8. Supplement Provides For: A revised Package Insert (PI).		
9. Pharmacological Category Antihypertensive	10. How Dispensed [X] Rx [ ] OTC	11. Related IND(s)/ NDA(s)/DMF(s)
12. Dosage Form(s) TCM	13. Potency(ies) 10/12.5, 20/12.5, 20/25 mg	
14. Chemical Name and Structure		15. Records/Reports Current [X] Yes [ ] No Reviewed [X] Yes [ ] No

16. Comments

This version of the PI provides for changes in the DOSAGE AND ADMINISTRATION section in compliance with letters from the Agency dated 29 Jan 97 and 18 Apr 97. The changes deal with dosage recommendations for hydrochlorthiazide.

The new version number and date are not provided.

No changes have been made in the technical aspects of the labeling, which remain satisfactory.

17. Conclusions and Recommendations

APPROVAL is recommended as far as the technical aspects of the labeling are concerned.

18. REVIEWER

Name James H. Short Signature James H. Short Date Completed 27 Oct 97

Distribution: [X] Original Jacket [ ] Reviewer [ ] Division File [ ] CSO

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R/D init:RWolters/

JWolters 10/27/97

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APPLICATION NUMBER: NDA 19-778/S-028

ADMINISTRATIVE DOCUMENTS

OCT 28 1998

RHPM Review of Labeling

NDA: 19-778/SLR-028 Zestoretic (lisinopril/HCTZ) Tablets

Date of submission: September 22, 1998

Date of receipt: September 28, 1998

Applicant: Merck Research Laboratories

Background: Merck has submitted final printed labeling in response to our Januray 7, 1998 approvable letter.

Review: The submitted final printed labeling has been revised as follows:

DOSAGE AND ADMINISTRATION:
The first sentence has been revised to read "Lisinopril is an effective treatment of hypertension in once-daily doses of 10-80 mg, while hydrochlorothiazide is effective in doses of 12.5-50 mg."

Recommendation: I will prepare an approval letter for this supplement. This supplement falls under 21 CFR 314.70 (b)(3) Supplements requiring FDA approval before the change is made.

Kathleen F. Bongiovanni

10-2-98

cc: 19-778/S-028
HFD-110
HFD-110/KBongiovanni
HFD-110/SBenton
HF-2/MedWatch
kb/10/2/98.

JAN -7 1998

RHPM Review of Labeling

NDA: 19-221/SLR-024 Vaseretic (enalapril maleate/HCTZ) Tablets
19-778/SLR-028 Prinzide (lisinopril/HCTZ) Tablets
20-387/SLR-006 Hyzaar (losartan potassium/HCTZ) Tablets

Date of submission: October 20, 1997

Date of receipt: October 23, 1997

Applicant: Merck Research Laboratories

Background: On January 29, 1997, we issued a Supplement Request Letter to all approved ACE inhibitor/hydrochlorothiazide products, saying "based on review of data that support the use of 12.5 mg HCTZ for the treatment of hypertension, including the recent approval of Microzide (HCTZ) 12.5 mg Capsules, we ask that you revise the DOSAGE AND ADMINISTRATION section of your package insert to state that HCTZ is an effective treatment of hypertension in doses of 12.5 - 50 mg per day."

On April 18, 1997, we issued Supplement Request letters to NDA 13-402 Aldoril (methyldopa/HCTZ), NDA 18-061 Timolide (timolol maleate/HCTZ), and NDA 11-958 Hydropres (reserpine/HCTZ), requesting revision of the DOSAGE AND ADMINISTRATION section by the replacement of the sentence "Patients usually do not require doses of hydrochlorothiazide in excess of 50 mg daily when combined with other antihypertensive agents." with "Hydrochlorothiazide can be given at doses of 12.5 to 50 mg per day when used alone."

Review: The submitted draft labeling has been revised as follows:

DOSAGE AND ADMINISTRATION:
The second sentence has been revised to read "The usual dosage range of enalapril is 10 to 40 mg per day administered in a single or two divided doses; hydrochlorothiazide is effective in doses of 12.5 to 50 mg daily." The following sentence has been added: "Patients usually do not require doses of hydrochlorothiazide in excess of 50 mg daily when combined with other antihypertensive agents."

According to Larry Bell, M.D., Merck added the sentence noted above so that the labeling for HCTZ-containing products would be consistent. I checked with Dr. Lipicky, and he said that he did not want that sentence added to these package inserts, and he would like to review the data from the NDAs that already have that sentence in their package inserts.

Recommendation: I will prepare an approvable letter for these supplements, asking for final printed labeling without the sentence "Patients usually do not require doses of hydrochlorothiazide in excess of 50 mg daily when combined with other antihypertensive agents." These supplements fall under 21 CFR 314.70 (b)(3) Supplements requiring FDA approval before the change is made.

Kathleen F. Bongiovanni

12-22-97

cc: 19-221/S-024
19-778/S-028
20-387/S-006
HFD-110 (all)
HFD-110/KBongiovanni
HFD-110/SBenton
HF-2/MedWatch
kb/12/22/97.