CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 19834/S009

MEDICAL REVIEW(S)

JUL 2 - 1997

Division of Cardio-Renal Drug Product
Medical Officer Review

NDA 19-834 S009

Name of Drug Plendil® (Felodipine) Extended Release Tablets

This correspondence is a counter-proposal by Astra-Merck to the FDA's proposed labeling.

Two changes are proposed by the sponsor:

1) Under PHARMACOKINETICS and METABOLISM the present FDA suggestion reads:

> "The bioavailability of PLENDIL is influenced by the presence of food. When administered either with a high fat or carbohydrate diet Cmax is increased by approximately 60%, AUC is unchanged.

The sponsor's suggestion is :

Comment: The sponsor's description is reasonable, AUC differs fasting and fed by < 10% so that the bioavailability does not seem to be modified. The sponsor seeks to add differentiation to the carbohydrate diet by re-adding the word high. The sponsor also seeks to emphasize the lack of change to AUC. These are not inaccurate, so that the sponsor's suggestion is acceptable.

The sponsor's suggestion I s:

Comment: The emphasis of the sponsor clearly is different than that of the FDA. The sponsor implies that PLENDIL is equally safe and effective taken with food or without food. Only as an afterthought is the type of food suggested. The change in

pharmacokinetics, however, with a high carbohydrate or high fat meal suggests that the drug is not likely to be a once-daily drug. Peak concentrations are increased, troughs depressed. None of the clinical studies were specifically done with food let alone a substantial diet. Safety, therefore is not guaranteed. I would prefer the FDAs but would include a reference to the CLINICAL PHARMACOLOGY, Pharmacokinetics and metabolism.)

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7/2/97

cc: NDA 19-834
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HFD-110/CSO