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APPLICATION NUMBER: NDA 20180/S11

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

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ORIGINAL

CLINICAL PHARMACOLOGY/BIOPHARMACEUTICS REVIEW

NDA: 20-180 SUBMISSION DATE: 02/15/96

Finasteride 5 mg tablets

BRAND NAME: Proscar

SPONSOR: Merck & Co., Inc REVIEWER: Tien-Mien Chen, Ph.D.

TYPE OF SUBMISSION: Supplement to An Approved NDA (Serial No. 011) Code: 1P

TITLE: "Review of Revision of Labeling Based on Additional Information/Study Results"

SYNOPSIS:

Merck's Proscar (finasteride 5 mg tablets) that was filed under original NDA 20-180 on 04/15/91 was previously reviewed by the Office of Clinical Pharmacology and Biopharmaceutics/Division of Pharmaceutical Evaluation II (OCPB/DPE II) on 02/10/92. The NDA was found acceptable and approved by the Agency on 06/19/92.

On 02/15/96, the sponsor submitted an NDA supplement for a revision of package insert (PI, 02/96 version) which was based on additional information/study results. Please see the PI in Attachment 1 for details. On 07/31/96, OCPB/DPE II was consulted by HFD-580 for review of the updated pharmacokinetic (PK) information of finasteride in the revised labeling.

Under "Pharmacokinetics" Subsection of the PI, only the last (7th) paragraph was revised based on the bioanalytical reports of Protocol Nos. 056 and 065. The above study results provided new data of the effects of finasteride levels on semen production in 124 male volunteers or on testosterone and dihydrotestosterone in scalp skin and sebum of 150 male volunteers. These studies employed a more sensitive assay method. The study reports of Protocol Nos. 056 and 065 have been reviewed by the medical officer, Dr. Fourcroy on 07/08/96 and the results were found acceptable by Dr. Fourcroy. Please see a copy of Dr. Fourcroy's review in Attachment 2 for details.

RECOMMENDATION:

Merck's supplement (Serial No. 011) for NDA 20-180 (Proscar; finasteride 5 mg tablets) that was submitted on 02/15/96 has been reviewed by OCPB/DPE II. The PK information included in the revised labeling is appropriate. However, FDA is currently attempting to standardize the content and presentation of the PK information that is included in the PI. Therefore, it is recommended that the PK subsection of the PI follow the format/template given in the Comment section below and the sponsor submit the revised PI to the Agency for review when the recommended changes are made.

COMMENT:(Needs to be sent to the sponsor)

The ***Pharmacokinetics*** portion should present information as appropriate under the subheadings of ***Absorption, Distribution, Metabolism, and Excretion***. Following this, there should be a section with the heading of ***Special Populations***, where pharmacokinetic information under the subheadings of ***Geriatric, Pediatric, Gender, Race, Renal Insufficiency, Hepatic Insufficiency, and Drug-Drug Interactions*** should be included. Where relevant information is lacking it should be so stated.

Lastly, a table(s) with mean (±SD) pharmacokinetic parameters determined under single and steady state conditions should be prepared. This table(s) should include bioavailability, peak concentration, time to peak, clearance, volume of distribution, half-life, and renal clearance for healthy subjects, and each special population including the drug's intended target population. Also, if appropriate a plot that illustrates drug plasma/serum concentration vs. time (i.e., different dosage strengths, comparison to a reference product, etc.) may be included.

/S/

08/05/96
Tien-Mien Chen, Ph.D.

Division of Pharmacokinetics Evaluation II

RD initialed by Angelica Dorantes, Ph.D. AD 08/05/96

FT initialed by Angelica Dorantes, Ph.D. 8/6/96 /S/

cc: NDA 20-180, HFD-580 (MO, CSO), HFD-870 (A. Dorantes. T. Chen), HFD-850 for C. Bott (Drug, Reviewer, Chron), HFD-340 (Viswanathan), HFD-205 (FOI).