CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-180/S-027

ADMINISTRATIVE DOCUMENTS

Division of Reproductive and Urologic Drug Products

PROJECT MANAGER LABELING REVIEW

Application Number: **NDA 20-180/SLR-027 Proscar** (finasteride) Tablets

Sponsor: Merck & Co., Inc.

Material Reviewed: NDA 20-180/SLR-027: Changes being effected supplement containing the package insert and patient package insert

Submission Date: August 15, 2003

Receipt Date: August 15, 2003

Background and Summary:

This product was approved for the treatment of symptomatic benign prostatic hyperplasia (BPH) in men with an enlarged prostate to:

- Improve symptoms
- Reduce the risk of acute urinary retention
- Reduce the risk of the need for surgery including transurethral resection of the prostate (TURP) and prostatectomy.

The sponsor has revised the package insert (PI) and patient package insert (PPI) to include new language that proposes:

1) Changes in the Labeling Section of the approved NDA to include isolated reports of male breast cancer in the ADVERSE REACTIONS, Long-Term Treatment.
2) Changes in the Information for Patients subsection of PRECAUTIONS to encourage physicians to instruct patients to promptly report any changes in their breasts, such as lumps, pain or nipple discharge, to their physician.
3) Changes consistent with those proposed in the PI under the "What you need to Know while taking PROSCAR" section of the PPI.

Review:

The labeling submitted in NDA 20-180/SLR-027 was compared to draft labeling submitted as electronic desk copies on July 18 and 21, 2003, in response to a teleconference held Jun2 13, 2003. Comparison was also made against final printed labeling submitted May 3, 2001 (SLR-022, FA). Other than the following changes to the PI and PPI, it was found to be identical:

- In the PRECAUTIONS section, the following new language (bold text for this review) was added as paragraph 10:

Physicians should instruct their patients to promptly report any changes in their breasts such as lumps, pain or nipple discharge. Breast changes including breast enlargement, tenderness and neoplasm have been reported (see ADVERSE REACTIONS).

- In the ADVERSE REACTIONS section, the following new language (bold text for this review) was added under a new section entitled "Long-Term Treatment"

  Long-Term Treatment

  - There is no evidence of increased adverse experiences with increased duration of treatment with PROSCAR. **New reports of drug-related sexual adverse experiences decreased with duration of therapy. The relationship between long-term use of finasteride and male breast neoplasia is currently unknown. During a 4- to 6-year placebo- and comparator-controlled study that enrolled 3047 men, there were 4 cases of breast cancer in men treated with finasteride but no cases in men not treated with finasteride. During the 4-year, placebo-controlled PLESS study that enrolled 3040 men, there were 2 cases of breast cancer in placebo-treated men, but no cases were reported in men treated with finasteride.**

- In the "What you need to know while taking PROSCAR" in the PPI, the following new language (bold text for this review) was added as paragraph 3 to bullet item 2:

  In addition, some men may have breast enlargement and/or tenderness. You should promptly report to your doctor any changes in your breasts such as lumps, pain or nipple discharge. Some men have reported allergic reactions such as rash, itching, hives, and swelling of the lips and face. Rarely, testicular pain has been reported.

Conclusions:

The submitted new language is identical to that agreed upon during label negotiations. An approval letter should be issued for the NDA 20-180/SLR-027.

{See appended electronic signature page}

Jean King, M.S., R.D.
PM, HFD-580

{See appended electronic signature page}

Margaret Kober, R.Ph.
Chief, Regulatory Project Management
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Drafted: JK 8/25/03

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/s/

Jean R. King
8/28/03 01:36:59 PM
CSO

Margaret Kober
8/29/03 01:52:38 PM
CSO
Chief, Project Management Staff

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-180

Merck & Co., Inc.
Attention: Vivian Fuh, M.D.
Director, Regulatory Affairs
P.O. Box 2000
RY 33-200
Rahway, NJ 07065-0900

Dear Dr. Fuh:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product:	PROSCAR™ (finasteride, 5 mg)
NDA Number:	NDA 20-180
Supplement number:	027
Date of supplement:	August 15, 2003
Date of receipt:	August 15, 2003

This supplemental application, submitted as "Supplement - Changes Being Effected," proposes changes in the Labeling Section of the approved NDA to include isolated reports of male breast cancer in the ADVERSE REACTIONS, Long-Term Treatment and for changes in the Information for Patients subsection of PRECAUTIONS to encourage physicians to instruct patients to promptly report any changes in their breasts, such as lumps, pain or nipple discharge, to their physician.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on October 14, 2003 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and research
Division of Reproductive and Urologic Drug Products, HFD-580
Attention: Document Room 8B-45
5600 Fishers Lane
Rockville, Maryland 20857

If you have any question, call Jean King, M.S., R.D., Regulatory Project Manager, at (301) 827-4260.

Sincerely,

{See appended electronic signature page}

Margaret Kober, R.Ph.
Chief, Regulatory Project Management
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Margaret Kober
8/29/03 01:51:12 PM
Chief, Project Management Staff