CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-788

ADMINISTRATIVE DOCUMENTS

ANDERSON
540

NDA 20-788

FEB 3 1997

Robert E. Silverman, M.D., Ph.D.
Merck Research Laboratories
Sunneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Dr. Silverman:

We have received your New Drug Application (NDA) submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Propecia (finasteride) 1 mg Tablet

Date of Application: December 20, 1996

Date of Receipt: December 20, 1996

Our Reference Number: NDA 20-788

Unless we find the application not acceptable for filing, the filing date will be February 18, 1997.

Please begin any communications concerning this application by citing the NDA number listed above. Should you have any questions concerning the NDA, please contact:

Robin Anderson
Project Manager
(301) 827-2023

Sincerely yours,

2/3/97

Mary Jean Kozma-Fornaro
Supervisor, Project Management Staff
Division of Dermatologic
and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation & Research

cc: Orig. NDA 20-788
HFD-92
HFD-540
HFD-540/CSO/Anderson
TECH/SMChilds/1/2/97
ACKNOWLEDGMENT LETTER

ITEM 13
PATENT AND EXCLUSIVITY INFORMATION
MERCK RESEARCH LABORATORIES

1)	Active Ingredient(s)	Finasteride
2)	Strength(s)	1 mg
3)	Trade Name	PROPECIA®
4)	Dosage Form, Route of Administration	Tablets, Oral
5)	Applicant Firm Name	Merck Research Laboratories
6)	NDA Number	20-788
7)	Approval Date	-
8)	Exclusivity - Date First ANDA could be approved	3 years from NDA approval date
	Length of Exclusivity Period	3 years
9)	Applicable patent numbers and expiration date of each	4,377,584 Expiration Date: 3/22/2000 4,760,071 Expiration Date: 6/19/2006 w/PTR 5,547,957 Expiration Date 10/15/2013 5,571,817 Expiration Date 11/5/2013

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NDA/PLA # 20-788 Supplement # NA Circle one: SE1 SE2 SE3 SE4 SE5 SE6

HFD-540 Trade (generic) name/dosage form: Propecia (finasteride) 1MG Action: (AP) AE NA

Applicant Merck Research Labs Therapeutic Class 35

Indication(s) previously approved NA

Pediatric labeling of approved indication(s) is adequate ____ inadequate ____

Indication in this application male pattern hair loss (androgenic alopecia), in MEN ONLY

(For supplements, answer the following questions in relation to the proposed indication.)

____ 1. **PEDIATRIC LABELING IS ADEQUATE.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric subgroups. Further information is not required.

____ 2. **PEDIATRIC STUDIES ARE NEEDED.** There is potential for use in children, and further information is required to permit adequate labeling for this use.

____ a. A new dosing formation is needed, and applicant has agreed to provide the appropriate formulation.

____ b. The applicant has committed to doing such studies as will be required.
- ____ (1) Studies are ongoing.
- ____ (2) Protocols were submitted and approved.
- ____ (3) Protocols were submitted and are under review.
- ____ (4) If no protocol has been submitted, explain the status of discussions on the back of this form.

____ c. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

X 3. **PEDIATRIC STUDIES ARE NOT NEEDED.** The drug/biologic product has little potential for use in children. Explain, on the back of this form, why pediatric studies are not needed.

____ 4. **EXPLAIN.** If none of the above apply, explain, as necessary, on the back of this form.

EXPLAIN, AS NECESSARY, ANY OF THE FOREGOING ITEMS ON THE BACK OF THIS FORM.

Signature of Preparer and Title (PM, CSO, MO, other) — 12-11-97 Date

cc: Orig NDA/PLA # 20-788
HFD-540 /Div File
NDA/PLA Action Package
HFD-510/GTroendle (plus, for CDER APs and AEs, copy of action letter and labeling)

12/19/97

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action.

5/95

The indication is for the treatment of male pattern baldness in men ages 18-40.

S Kummerer
Proj. Man.
12-11-97

12/9/97

JUN 2 0 1997

Memorandum

To: Ella Toombs, M.D., Acting Dermatology Team Leader

From: Hon-Sum Ko, M.D., Medical Officer

Re: NDA 20-788 - Proposed Study with Neutrogena Shampoos

The Applicant of this NDA (PROPECIA™) submitted a draft protocol on 5/13/97, which is due to start in the next 4-6 weeks.

Title: An open, randomized, two period, cross-over study to evaluate the effect of a tar-based shampoo (Neutrogena T/Gel®) on hair counts in men with male pattern hair loss.

Objective: To estimate the difference in hair counts after shampooing with a tar based vs a non-tar based shampoo in men with male pattern baldness.

Background: The clinical studies in this NDA were done in men with male pattern baldness. The patients were required to use Neutrogena T/Gel® shampoo as part of the protocol routine in order to prevent the development of seborrheic dermatitis, which might affect counting of hair. During the 90-day meeting for this NDA, the Applicant was asked whether the use of the medicated shampoo with tar would affect the hair count because of the possibility that the vellus hairs might be made more prominent and get more easily counted. This proposed study is a response to that question.

Design: Single-center, open, randomized, two-treatment, two-period crossover study with each treatment for 7 days shown as follows -

Regimen	Day 0	Days 1-7	Day 7	Days 8-14	Day 14
A	Hair Ct	Use X*	Hair Ct	Use Y	Hair Ct
B	Hair Ct	Use Y	Hair Ct	Use X	Hair Ct

*X=Neutrogena® Anti-residue Shampoo, Y=Neutrogena T/Gel® Shampoo.

Patient Sample: 40 males with Modified Norwood Hamilton Classification Grade II vertex, III vertex, IV or V with moderate vertex hair loss and aged 18-40.

Evaluations: Hair counts - computer-assisted counts of dot mapped macrophotographs of a defined, 1-inch diameter circular area of the scalp taken at baseline, day 7 and day 14. The validated dot-mapper(s) [technicians] will be blinded to subject, treatment and time.

Data Analysis: The difference in hair counts on day 7 and day 14 will be compared between the two treatment regimens with ANOVA.

Comments

1. This study uses a medicated shampoo vs a non-medicated shampoo. Although it involves investigational use of a

marketed "drug", this is an approved use of the shampoo and has no violation of the "interstate commerce" clause.
2. There are no safety concerns.
3. IRB approval would still be needed for protection of human subjects.
4. This protocol does not have a washout period. It is unclear whether staining by tar will remain after 7 days of use with the Neutrogena Anti-residue Shampoo. The Applicant needs to address this.
5. The protocol should prohibit the use of any drugs or procedures that may affect hair counts during the study period.
6. The hair is not clipped after the first hair-counting, There is a possibility that the increase in length of some hairs may affect counting in the second reading.
7. The Applicant has not addressed the question whether the methodology of hair counting included vellus hair in their counts for the pivotal clinical trials:
(i) If they were to be excluded, then this study provides an opportunity to see whether staining by a tar shampoo would affect the counts by making vellus hair more prominent and counted falsely as terminal hair.
(ii) If they were not to be excluded in counting during the clinical trials, this study may allow estimation of whether previous counts were falsely low by not including vellus hairs that were missed because of poor visibility.
It must be stressed that success in treatment should be judged by growth of terminal hair and not vellus hair.

Reommendations: The Applicant should address the above comments but the protocol may proceed upon IRB approval.

6/22/97

c.c. NDA 20-788
Div File
HFD-540 Div Dir/Wilkin
HFD-540 CSO/Anderson
HFD-725 Biometrics/Freidlin

6/20/97

DEC 16 1997

Memorandum

Date: December 3, 1997

To: Jonathan Wilkin, M.D.
Director, DDDDP (HFD-540)

Through: Abby Jacobs, Ph.D. 12/16/97
Team Leader, DDDDP (HFD-540)

From: Javier Avalos, Ph.D. 12/14/97
Pharmacologist/Toxicologist, DDDDP (HFD-540)

RE: NDA 20-788 (Propecia): Sponsor's Response to Label Recommendations

On December 2, 1997, Merck Research Laboratories submitted their response to the Agency's suggested text for the product circular and patient package insert for Propecia. The Sponsor rejected our suggestions for the Carcinogenicity and Pregnancy Sections. MRL justification is that they believe it is inappropriate and confusing to the prescriber to have inconsistency in the presentation of information between the Propecia and Proscar labeling. Within each label, the comparison of human exposure to animal findings are based sometimes on dose equivalents and other times on systemic exposure, which I find confusing. I am recommending that the Sponsor use systemic exposure when calculating the human equivalent, which has been determined to be more accurate than extrapolations based on body weight or body surface area (Viosin *et al.* Regulatory Toxicology and Pharmacology 1990; 12:107-116). Additionally, the ONLY difference between the two labels in these sections is the comparisons to human exposure, which needs to be different in the first place since the human dosages differ for Propecia and Proscar. I fail to understand how the prescriber would be confused between both labels if the only difference between our suggested text and that of Proscar is what is supposed to be different between the two labels. Thus, my recommended suggestions for the Carcinogenesis and Pregnancy Category sections remain unchanged.

<u>Recommended Changes to Propecia Label:</u>

Redacted 1

pages of trade

secret and/or

confidential

commercial

information

cc:
NDA 20-788
HFD-540/CSO/Kummerer
HFD-880/Biopharm/Bashaw
HFD-880/Biopharm/Kumi
HFD-540/MO/Ko
HFD-540/MO/Walker
HFD-540/Chem/Hathaway
HFD-540/Chem/DeCamp
HFD-540/Pharm/Jacobs