

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-834

ADMINISTRATIVE DOCUMENTS

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NDA/PLA # 20834 Supplement # _____ Circle one: SE1 SE2 SE3 SE4 SE5 SE6

HFD 540 Trade (generic) name/dosage form: Regain Extra strength for men (minoxidil) 5%/6 Action: AP AE NA

Applicant Pharmacia Upjohn Therapeutic Class HAIR Regrowth Stimulant

Indication(s) previously approved none for this strength
Pediatric labeling of approved indication(s) is adequate inadequate NA

Indication in this application HAIR Regrowth Treatment for men
(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.
- 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. For use by men 18 years of age and greater
- 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) _____ Date 11/12/97

11/14/97
11/14/97

cc: Orig NDA/PLA # 20834
HFD 540 /Div File
NDA/PLA Action Package
HFD-510/GTroendle (plus, for CDER APs and AEs, copy of action letter and labeling)

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.

Androgenetic alopecia
is rare in pediatric
patients,

11/14/17

DEBARMENT CERTIFICATION FOR 5% MINOXIDIL TOPICAL SOLUTION

Pursuant to section 306(k)(1) of the Federal Food, Drug and Cosmetic Act, the applicant certifies that, to the best of its knowledge and belief, the applicant did not and will not use in any capacity the services of any person listed pursuant to section 306(e) as ~~debarred~~ under subsections 306(a) or (b) of the Act in connection with this application.

Ed L. Patt
Manager
Regulatory Compliance

January 24, 1997

Date

NDA 20-834
5% Minoxidil Topical Solution

XIII. PATENT INFORMATION

PATENT CERTIFICATION

- | | | |
|----|--|---|
| 1. | Active Ingredient | Minoxidil |
| 2. | Strength(s) | 5% |
| 3. | Trade Name | To be determined |
| 4. | a. Dosage Form | Solution |
| | b. Route of Administration | Topical |
| 5. | Applicant Firm Name | Pharmacia & Upjohn Company |
| 6. | NDA Number | 20-834 |
| 7. | NDA Approval Date | To be determined |
| 8. | Exclusivity - Date first ANDA could be approved and length of exclusivity period | Three (3) years after date of NDA approval. |
| 9. | Applicable patent numbers and expiration date of each | None |

This is to certify that the above information is correct to the best of my knowledge.

Raymond E. Dann, Ph.D.
Director, OTC Regulatory Affairs

Consult #897 (HFD-540)

ROGAINE EXTRA STRENGTH FOR MEN

minoxidil 5% topical solution

ROGAINE is an established trademark for these products and was not evaluated by the Committee. The "EXTRA STRENGTH FOR MEN" was questioned to find out if women may use this product also. The reviewing division assured the LNC that the product was only approvable for men and would be prominently labeled as such. Therefore, the Committee finds no misleading aspects in the proposed name.

The Committee has no reason to find the proposed proprietary name unacceptable.

11/7/97, Chair
CDER Labeling and Nomenclature Committee

Food and Drug Administration
Detroit District
1560 East Jefferson Avenue
Detroit, MI 48207-3179
Telephone: 313-226-6260

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

July 2, 1996

Ley Smith, President
Kalamazoo Pharma Products Center
Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, MI 49001-0199

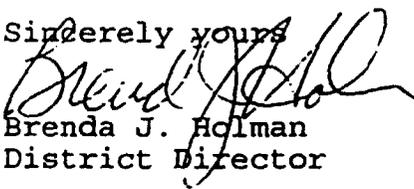
Regarding:
NDA Rogaine-5 Topical Solution

Dear Mr. Smith:

This letter is written to advise you that Detroit District has recommended to our Center for Drug Evaluation and Research that NDA be approved. We have made this decision based upon the June 4-6, 1996 inspection of your plant which concentrated upon the manufacturing of the referenced product.

Our Center for Drug Evaluation and Research will make their evaluation and notify your firm accordingly.

Sincerely yours


Brenda J. Holman
District Director

REGULATORY AFFAIRS

JUL 23 1996

PPC U.S.

RECEIVED

JUL 08 1996

LSS

FORWARD PLANNING MEETING SUMMARY

DATE: 4/14/97

PARTICIPANTS FROM FDA:

HFD-540:

Jonathan Wilkin, M.D., Division Director
Janet Higgins, M.S., Chemist (for Steve Hathaway)
Javier Avalos, Ph.D, Pharmacologist/Toxicologist
Robin Anderson, R.N., M.B.A., Project Manager
Mary Jean Kozma-Fornaro, R.N, M.S., Supervisory Project Manager

HFD-725:

R. Srinivasan, Ph.D, Supervisor, Biostatistics
Shala Farr, Ph.D, Biostatistician

HFD-880:

Dennis Bashaw, Ph.D, Biopharmaceutical Team Leader

HFD-560:

Linda Katz, M.D., Deputy Clinical Director
Steve Aurecchia, M.D., Medical Reviewer
Nahid Mokhtari-Rejali, Ph.D, Chemist
Rosemary Cook, M.B A., Supervisory Project Manager
Carol Doyle, Project Manager

HFD-40:

Karen Lechter, Social Science Analyst

**SUBJECT: Rogaine Extra Strength for Men (minoxidil solution, 5%) Topical Solution, 5%,
NDA 20-834**

OBJECTIVE: To determine the fileability of NDA 20-834

The meeting was convened to determine the adequacy of NDA 20-834 for filing. All sections of the New Drug Application (NDA) were evaluated in terms of the general content and format requirements. The application was deemed fileable, pending the receipt of statements from the applicant concerning (1) the facilities are ready for inspection and (2) clarifying the release of environmental assessment information by FOI. Applicant was contacted by phone immediately after the meeting and agreed to submit these statements to the NDA ASAP.

Robin Anderson, Project Manager, HFD-540

Attachments (Checklists)

cc:

NDA 20-834

HFD-540/Division File

HFD-540/Wilkin

HFD-540/Huene

HFD-540/DeCamp

HFD-540/Hathaway

HFD-540/Jacobs

HFD-540/Avalos

HFD-540/Kozma-Fornaro 5/12/97

HFD-540/Anderson

HFD-725/Srinivasan

HFD-725/Farr

HFD-880/Bashaw

HFD-40/Lechter

HFD-560/Bowen

HFD-560/Katz

HFD-560/Aurecchia

HFD-560/Mokhtari-Rejali

HFD-560/Cook

HFD-560/Doyle

120150

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FORWARD PLANNING MEETING CHECKLIST

April 14, 1997

NDA 20-834

**Rogaine Extra Strength For Men (minoxidil topical solution, 5%) Topical Solution, 5%
androgenetic alopecia**

Pharmacia and Upjohn

Type 3S

Filing Date: 4/29/97

User Fee Date: 2/2/8/98

Regulatory Due Date: 8/27/97 (review promised by this date)

Target date: 7/97

FILEABILITY:

On initial overview of the NDA application:

PROJECT MANAGEMENT:

(1) Do any of the following apply to this application (i.e., if YES , the application MUST BE REFUSED TO FILE under 314.101 (e) and there is no filing over protest):

(a) Is the drug product already covered by an approved application?

NO.

(b) Does the submission purport to be an abbreviated application under 314.55; however the drug product is not one for which FDA has made a finding that an abbreviated application is acceptable under 314.55(b)?

NO.

(c) Is the drug product subject to licensing by FDA under the Public Service Act and Subchapter F of Chapter I of Title 21 of the CFR?

NO.

(2) Do any of the following apply to this application (i.e., if NO, the application MAY BE REFUSED TO FILE under 314.101(d) and there is the potential for filing over protest):

(a) Does the application contain a completed application form as required under 314.50 or 314.55?

YES.

(b) On its face, does the application contain the sections of an application required by regulation and Center guidelines?

• Clinical • Biopharm • Chemistry

• Pharm/Tox • Statistics

YES.

C) Has the applicant submitted a complete environmental assessment which addresses each of the items specified in the applicable format under 25.31 or has the applicant submitted evidence to establish that the product is under 25.24 of the CFR?

YES, in Vol. 1.4 and 1.5

(d) On its face, is the NDA formatted in compliance with Center guidelines including integrated efficacy and safety summaries?

YES. Integrated efficacy and safety summaries are located in vol. 1.2.

(e) Is the NDA indexed and paginated?

YES.

(f) On its face, is the NDA legible?

YES.

(g) Has the applicant submitted all required copies of the submission and various sections of the submission?

YES.

(h) Has the sponsor submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor?

YES, as of 4/11/97.

(I) Does the application contain a statement that all nonclinical laboratory studies were conducted in compliance with the requirements set forth in Part 58 or a statement why a study was not conducted in compliance with those requirements?

YES, located in individual study reports.

(j) If required, has the applicant submitted carcinogenicity studies?

YES, in vol. 1.6.

(k) On its face, does the application contain at least two adequate and well-controlled clinical trials?

YES, pivotal studies are located in volume 1.2, pg. 2/1/138: M/7410/0285, M/7410/0286, M/7415/0001 and M/7415/0009. All studies test Minoxidil solution 5% vs. Minoxidil 2% vs. Placebo. All studies conducted in the U. S.

(l) Does the application contain a statement that all clinical trials were conducted in accord with the IRB/Declaration of Helsinki provisions of the CFR?

YES, located in vol. 1.88, pg. 8/8/2

20-834

- (m) Have all articles/study reports been submitted whether in English or translated into English?
YES.
- (n) Has the applicant submitted draft labeling in compliance with 210.56 and 210.57 of the CFR?
YES, copy of label provided to all reviewers.
- (o) Has the applicant submitted the required FRAUD POLICY notice?
YES, see debarment statement located in vol. 1.2.
- (p) Has the applicant submitted copies of all package inserts (or their equivalent) from all countries in which this product has been previously approved for marketing? Have all non-English package inserts been translated?
Yes, foreign approval/marketing history is located in vol. 1.2, pg. 2/1/39. A side-by-side comparison of the approved topical Minoxidil solution 2% to the proposed Minoxidil solution 5% is located in vol. 1.2, pg. 2/1/1.
- (q) Has the applicant stated that the integrated summary of safety includes all safety data for this product of which they are aware from all sources, domestic and foreign? What is the cut-off date for the preparation of the ISS?
YES, cut off date listed as 3/31/95.
- (r) If this is a CANDAs submission, has the applicant submitted a statement to the archival NDA that the text, tables, and data in the CANDAs and the archival hard copy NDA are identical? If they are not identical, is there a letter to the archival NDA that specifies distinctly ALL of the differences in the two submissions?
N/A
- (3) From a project management perspective, is this NDA fileable? If "no". please state on the reverse why it is not.
YES.

4/11/97
Project Manager

4/11/97
Supervisory Project Manager

NDA FORWARD PLANNING MEETING CHECKLIST

FILEABILITY: NDA 20-834, ROGAINE[®] Extra Strength for Men (5% minoxidil topical solution)

On initial overview of the NDA application:

YES NO

CHEMISTRY, MANUFACTURING AND CONTROLS:

- (1) On its face, is the CMC section of the NDA organized in a manner to allow substantive review to begin? -X-
- (2) Is the CMC section of the NDA indexed and paginated in a manner to allow substantive review to begin? -X-
- (3) On its face, is the CMC section of the NDA legible so that substantive review can begin? -X-
- (4) Are all the facilities (manufacturing, packaging, testing, sterilization, etc.) appropriately delineated with full addresses? -X-
- (5) Has the applicant provided a statement certifying that all facilities listed in the application are currently ready for inspection? -X-
- (6) Has the applicant submitted a complete environmental impact assessment? -X-*
- (7) Has the applicant developed appropriate controls assessment procedures that are currently ready for FDA verification? -X-
- (8) For an antibiotic, has the applicant submitted an appropriate validation package and committed to the readiness of exhibit samples? N/A
- (9) Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor? -X-
- (10) Has the applicant submitted draft labeling consistent with 21 CFR 201.56 and 201.57, current Division labeling policies, and the design of the development package? -X-
- (11) Has the applicant submitted stability data to support and justify the proposed expiry? -X-
- (12) From a manufacturing and controls perspective, is this NDA fileable? If "No," please state on reverse why it is not. -X-

Reviewing Chemist 4/9/97

Supervisory Chemist 4/9/97 for

* Company should submit statement clarifying the release of EA information by FOI. They should list page #s in EA.

AUGUST 1997

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Division of Dermatologic and Dental Drug Products (HFD-540)
Pharmacology/Toxicology Forward Planning Meeting

NDA Number: 20-834 **Date:** April 14, 1997
Drug Name: Minoxidil (5%) **Reviewer:** Javier Avalos
(Rogaine)
CAS Number: 38304-91-5
Drug Type: New Concentration (i.e. NME, new formulation, new indication)
Drug Class: Anti-androgenic
Indication: For the treatment of androgenic alopecia
Route of Administration: Topical
Date CDER Received: March 3, 1997
User Fee Date: ~~March 3, 1998~~ AUGUST 17, 1997
Expected Date of Draft Review: May 20, 1997

Sponsor: Pharmacia & UpJohn Company
700 Portage Road
Kalamazoo, Michigan 49001-0199
(616) 833-5612

Fileability:

On initial overview of the NDA application:

YES NO

- (1) On its face, is the pharmacology/toxicology section of the NDA organized in a manner to allow substantive review to begin?
Comments? X _____
- (2) Is the pharm/tox section of the NDA indexed and paginated in a manner to allow substantive review to begin? X _____
- (3) On its face, is the pharm/tox section of the NDA legible so that substantive review can begin? X _____
- (4) Are all required (*) and requested IND studies completed and submitted in this NDA (carcinogenicity, mutagenicity, teratogenicity*, effects on fertility*, juvenile studies, acute studies*, chronic studies*, maximum tolerated dosage determination, dermal irritancy, ocular irritancy, photocarcinogenicity, animal pharmacokinetic studies, etc)?
Comments? X _____

- (5) If the formulation to be marketed is different from the formulation used in the toxicology studies, has the Sponsor made an appropriate effort to either repeat the studies using the to-be-marketed product or explained why such repetition should not be required?
Comments? X
- (6) Are the proposed labeling sections relative to pharm/tox appropriate (including human dose multiples expressed in either mg/m² or comparative serum/plasma levels) and in accordance with 201.57?
Comments? The label is an OTC label. X
- (7) Has the Sponsor submitted all special studies/data requested by the Division during pre-submission discussions with the Sponsor?
Comments? X
- (8) On its face, does the route of administration used in the animal studies appear to be the same as the intended human exposure route? If not, has the Sponsor submitted a rationale to justify the alternative route? X
- (9) Has the Sponsor submitted a statement(s) that all of the pivotal pharm/tox studies have been performed in accordance with the GLP regulations (21 CFR 58) or an explanation for any significant deviations?
Comments? X
- (10) Has the Sponsor submitted the data from the nonclinical carcinogenicity studies, in the STUDIES electronic format, for the review* by Biometrics?
Comments? X
- These studies were submitted in the withdrawn NDA 20-492.
- (11) Has the Sponsor submitted a statement(s) that the pharm/tox studies have been performed using acceptable, state-of-the-art protocols which also reflect agency animal welfare concerns?
Comments? X

45 DAY MEETING CHECKLIST

FILEABILITY:

On initial overview of the NDA application:

YES

NO

CLINICAL:

- (1) On its face, is the clinical section of the NDA organized in a manner to allow substantive review to begin?
- (2) Is the clinical section of the NDA indexed and paginated in a manner to allow substantive review to begin?
- (3) On its face, is the clinical section of the NDA legible so that substantive review can begin?
- (4) If needed, has the sponsor made an appropriate attempt to determine the most appropriate dosage and schedule for this product (i.e., appropriately designed dose-ranging studies)?
- (5) On its face, do there appear to be the requisite number of adequate and well-controlled studies in the application?
- (6) Are the pivotal efficacy studies of appropriate design to meet basic requirements for approvability of this product based on proposed draft labeling?
- (6) Are all data sets for pivotal efficacy studies complete for all indications (~~infections~~) requested?
- (7) Do all pivotal efficacy studies appear to be adequate and well-controlled within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?
- (8) Has the applicant submitted line listings in a format to allow reasonable review of the patient data? Has the applicant submitted line listings in the format agreed to previously by the Division?

(Y)

(Y)

(Y)

(Y)

(Y)

(Y)

(Y)

(Y)

(Y)

- (9) Has the application submitted a rationale for assuming the applicability of foreign data (disease specific microbiologic specific) in the submission to the US population?
- (10) Has the applicant submitted all additional required case record forms (beyond deaths and drop-outs) previously requested by the Division?
- (11) Has the applicant presented the safety data in a manner consistent with Center guidelines and/or in a manner previously agreed to by the Division?
- (12) Has the applicant presented a safety assessment based on all current world-wide knowledge regarding this product?
- (13) Has the applicant submitted draft labeling consistent with 201.56 and 201.57, current divisional policies, and the design of the development package?
- (14) Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor?
- (15) From a clinical perspective, is this NDA fileable? If "no", please state below why it is not.

N/A

(Y)

(Y)

(Y)

N/A

(Y)

(Y)

If certain claims are not filable, please state which claims they are and why they are not filable.

2/14/97

Reviewing Medical Officer

2/14/97

Supervisory Medical Officer

FORWARD PLANNING/FILEABILITY MEETING

NDA 20-834

Rogaine 5% Topical Solution for Men (Minoxidil Solution, 5%)

Hair Regrowth

Pharmacia & Upjohn Company

Type: 3S

Filing Date: April 29, 1997

User Fee Date: February 28, 1998

Regulatory Due Date: August 27, 1997

Target Date: July, 1997

FILEABILITY

On initial overview of the NDA application:

YES NO

PROJECT MANAGEMENT:

(1) Do any of the following apply to this application (i.e., if YES, the application MUST BE REFUSED TO FILE under 314.100(e) and there is no filing over protest):

- | | |
|--|----|
| (a) Is the drug product already covered by an approved application? | NO |
| (a) Does the submission purport to be an abbreviated application under 314.55; however the drug product is not one for which FDA has made a finding that an abbreviated application is acceptable under 314.55(b)? | NO |
| (b) Is the drug product subject to licensing by FDA under the Public Service Act and Subchapter F of Chapter I of Title 21 of the CFR? | NO |

(2) Do any of the following apply to this application (i.e., if NO, the application MAY BE REFUSED TO FILE under 314.100(d) and there is the potential for filing over protest):

- | | |
|--|-----|
| (a) Does the application contain a completed application form as required under 314.50 or 314.55? | YES |
| (b) On its face, does the application contain the sections of an application required by regulation and Center guidelines? | YES |
| (c) Has the applicant submitted a complete environmental assessment which addresses each of the items specified in the applicable format under 25.31 or has the applicant submitted evidence to establish that the product is subject to categorical exclusion under 25.24 of the CFR? | YES |

Rogaine 5% Topical Solution for Men (5% Minoxidil Topical Solution)

- | | |
|---|----------|
| (d) On its face, is the NDA formatted in compliance with Center guidelines including integrated efficacy and safety summaries? | YES |
| (e) Is the NDA indexed and paginated? | YES |
| (f) On its face, is the NDA legible? | YES |
| (g) Has the applicant submitted all required copies of the submission and various sections of the submission? | YES |
| (h) Has the sponsor submitted all special studies/data requested by the Division during Pre-submission discussions with the sponsor? | YES |
| (i) Does the application contain a statement that all non-clinical laboratory studies was conducted in compliance with the requirements set forth in Part 58 or a statement why a study was not conducted in compliance with those requirements? | YES |
| (j) If required, has the applicant submitted carcinogenicity studies? | YES |
| (k) On its face, does the application contain at least two adequate and well-controlled clinical trials? <i><u>Protocol M/7415/0001</u> "Efficacy and Safety Study of 5% TMS vs TMS and PBO"</i> <i><u>Protocol M/7410/0285</u> "Efficacy and Safety Study of 5% TMS vs 2% TMS and PBO"</i> | YES |
| (l) Does the application contain a statement that all clinical trials were conducted in accord with the IRB/Declaration of Helsinki provisions of the CFR? | YES — |
| (m) Have all articles/study reports been submitted either in English or translated into English? | YES |
| (n) Has the applicant submitted draft labeling in compliance with 210.56 and 210.57 of the CFR? | YES |
| (o) Has the applicant submitted the required FRAUD POLICY notice? | YES |
| (p) Has the applicant submitted copies of all package inserts (or their equivalent) from all countries in which this product has been previously approved for marketing? Have all non-English package inserts been translated? | YES |

Rogaine 5% Topical Solution for Men (5% Minoxidil Topical Solution)

(r) If this is a CANDA submission, has the applicant submitted a statement to the archival NDA that the text, tables, and data in the CANDA and the archival hardcopy NDA are identical? If they are not identical, is there a letter to the archival NDA that specifies distinctly ALL of the differences in the two submissions? N/A

(3) From a project management perspective, is this NDA fileable? If "no", please state on reverse why it is not. YES

Carol Doyle
Project Manager
Division of OTC Drug Products (HFD-560)

4/15/97

Date

Rosemary Cook
Supervisory Project Manager
Division of OTC Drug Products (HFD-560)

4/15/97

Date

ce
Orig NDA 20-834
File
HFD-560/M. Wright