CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-812

CHEMISTRY REVIEW(S)

Table of Contents

Chemistry Review Data Sheet

1. NDA 21-812

2. REVIEW #: 1

3. REVIEW DATE: 11/18/05

4. REVIEWER: Vispi P. Bhavnagri

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
None	NA

6. SUBMISSIONS BEING REVIEWED:

Submissions Reviewed	Document Date
NDA 21-812	3/25/05
Amendment (BC)	10/26/05
Amendment (BC)	12/22/05
Amendment (BC)	1/13/06
Amendment (BC)	1/18/06

7. NAME & ADDRESS OF APPLICANT:

Name: Pfizer Inc.

Address: 201 Tabor Road, Morris Plains, NJ 07950

Representative: Dina R. Russelo, Dir. Reg. Affairs

Telephone: 973-385-4909

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Men's Rogaine® Extra Strength
b) Non-Proprietary Name (USAN): minoxidil

c) Code Name/# (ONDC only): PNU-10858
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505(b)

10. PHARMACOL. CATEGORY: Hair growth promoter

11. DOSAGE FORM: Topical Aerosol

12. STRENGTH/POTENCY: 5%

13. ROUTE OF ADMINISTRATION: Topical

14. Rx/OTC DISPENSED: ___Rx X OTC

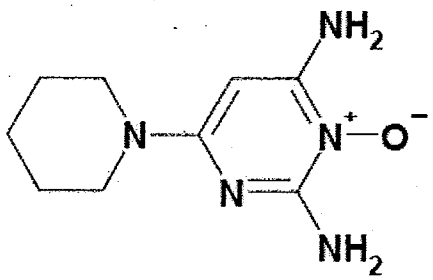
15. **SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):**

_____SPOTS product – Form Completed

__X__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

2,4-pyrimidinediamine, 6-(1-piperidinyl)-,3-oxide
Molecular Formula: $C_9H_{15}N_5O$
Molecular Weight: 209.25



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	Type	Holder	Item Referenced	Code[1]	Status[2]	Dt. Review Completed	Comments
					NA	NA	----------
					NA	NA	----------
					NA	NA	----------
					NA	NA	----------
					NA	NA	----------

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

Document	Application Number	Description
NDA	19-501	2% Topical Minoxidil Solution
NDA	20-834	5% Topical Minoxidil Solution

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	NA	NA	NA
EES	Acceptable	11/16/05	J.D Ambrogio
Pharm/Tox	NA	NA	NA
Biopharm	NA	NA	NA
LNC	NA	NA	NA
Methods Validation	NA	NA	NA
OPDRA	NA	NA	NA
EA	NA	NA	NA
Microbiology	NA	NA	NA

Zip #3\Review\NDA 21-812-Rev

Appears This Way
On Original

The Chemistry Review for NDA 21-812

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

From the CMC standpoint, recommend **approval.**

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

NA

II. Summary of Chemistry Assessments

A. Description of the Drug Product and Drug Substance

Drug Substance

This NDA references NDA 19-501 for the drug substance minoxidil. The following information on minoxidil is excerpted from the twelfth edition of the Merck Index.

Minoxidil is a crystalline powder with a melting point of 248° C. It has a pKa of 4.61, and its solubility in some common solvents is reproduced in the following table.

Solvent	Solubility (mg/mL)
Propylene glycol	
Methanol	
Ethanol	
DMSO	
Water	
Chloroform	
Acetone, EA, ACN, etc,	

The drug substance is an antihypertensive and used as an antialopecia agent.

Drug Product

The applicant has named the drug product as a "Foam." However, foam is not recognized as a dosage form according to the USP, the Orange Book or the CDER Data Standards Manual on dosage forms.

After consultation with various people (Ms. Yanna Mille, Ms. Sue-Ching Lin, Dr. Guirag Poochikian, etc.) it was determined by Dr. John Smith that the most appropriate name for the drug product is "Topical Aerosol", since the product (1) contains a propellant and (2) will be used topically.

The drug product contains 5% minoxidil and comes in three versions; a non-scented version and two scented versions (Sport Fragranced and Floral Fragranced).

The drug product is manufactured in two phases, an ____ phase and a ____ phase. The drug substance is contained in the ____ phase.

B. Description of How the Drug Product is Intended to be Used

The container closure has a child resistant cap that snaps onto the dispensing valve. The cap is placed into the palm of a hand. An amount equivalent to half a capful of the drug product is dispensed on to the fingertips of the same hand using the cap as a gauge. The dispensed amount is then applied to the scalp. This procedure is to be repeated twice a day. Since each can has 60 g of the drug product and this amount is sufficient for a

month, in theory, 2 g of the DP are applied daily to the scalp. The minoxidil concentration in the topical aerosol is 5%. Therefore the daily dose is 100 mg in two divided doses of 50 mg each.

C. Basis for Approvability or Not-Approval Recommendation

Recommend approval since (1) the application does not have any remaining CMC deficiencies (2) the stability data is satisfactory and (3) the EER is acceptable

One key issue that had to be resolved during the review concerned the yellowing of the product on stability. In the amendment dated 10/26/05 the company revised the color description for samples on stability, indicating that more of a change in color was taking place on storage than had been evident before. Since the [redacted] terms were vague, the company was asked for a less subjective test to describe the color of the drug product. The company proposed a color comparison test, in which the liquefied drug product (the "foam" collapses or melts at [redacted] would be compared to a set of standard colored solutions. The company proposed a limit of not more than [redacted]. However, since this was based on the color observed for very aged samples stored under accelerated storage conditions [redacted] this was not considered acceptable. After negotiation the company proposed to have one acceptance color criterion for samples stored at [redacted] RH (NMT standard [redacted] and another for samples stored at [redacted] RH (NMT standard [redacted] This is acceptable.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

Chemist Name/Date: Vispi P. Bhavnagri
Secondary Reviewer ~~Chemistry Team Leader~~: John Smith/Date
Project Manager: Tia Frazier

C. CC Block

45 Page(s) Withheld

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_____ Draft Labeling

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Withheld Track Number: Chemistry-1

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/s/

Vispi Bhavnagri
1/19/2006 02:01:41 PM
CHEMIST

John Smith
1/19/2006 02:09:00 PM
CHEMIST

2 Page(s) Withheld

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Withheld Track Number: Chemistry- 2