CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 075357

Name: Minoxidil Topical Solution USP, 2%

Sponsor: L. Perrigo Company

Approval Date: July 30, 1999

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 075357

CONTENTS

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Administrative & Correspondence Documents	**X**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 075357

APPROVAL LETTER

ANDA 75-357

JUL 30 1999

L. Perrigo Company
Attention: Brian R. Schuster
117 Water Street
Allegan, MI 49010

Dear Sir:

This is in reference to your abbreviated new drug application dated April 13, 1998, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Minoxidil Topical Solution USP, 2% (for Men) and Minoxidil Topical Solution USP, 2% (for Women).

Reference is also made to your amendments dated February 18, May 19, July 9, and July 27, 1999.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted over-the-counter (OTC) labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Minoxidil Topical Solution USP, 2% (for Men) and your Minoxidil Topical Solution USP, 2% (for Women) to be bioequivalent to the listed drug (Rogaine® for Men and Rogaine® for Women, respectively, of Pharmacia and Upjohn Co.).

Under 21 CFR 314.70, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Sincerely yours,

Gary Buehler for 7/30/99

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-357
Division File
FIELD COPY
HFD-610/R.West
HFD-92
HFD-210/B.Poole
HFD-330/

Endorsements:
HFD-629/K.Woodland/ K.Woodland 5/25/99 7/16/99
HFD-629/P.Schwartz/ PS 5/25/99 PS 7/16/99
HFD-617/J.Buccine/5/25/99 gp 5/26/99 7-16-99
HFD-613/L.Golson/ L.Golson 5/26/99
HFD-613/J.Grace/ 5/26/1999

X:\NEW\FIRMSNZ\PERRIGO\LTRS&REV\75357.AP
F/T by: gp/5/25/99

APPROVAL

Robert Lyle Lett 7/30/99

7/27/99

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 075357

LABELING

Instructions for use of Applicators
APPLICATOR OPTIONS
Hair styles and degree of hair loss can be very different for each person. We have included two applicators that have been designed especially for men. You can choose whichever one works best for you.

A. DROPPER
The child resistant dropper can be useful for a broad range of hair styles or hair loss because it allows for easy application through the hair and directly onto the scalp.

B. SPRAYER
This may be more useful for broader areas of hair loss.

Using the Applicators

A. DROPPER

1. Squeeze the rubber bulb and insert the dropper into the bottle. Release the bulb, allowing the dropper to fill to the 1 mL line. If the level of the solution is above the 1 mL line, squeeze the extra amount back into the bottle.

2. Next, place the tip near the part of the scalp you want to treat and gently squeeze the bulb to gradually release the solution. To prevent the solution from running off the scalp, apply a small amount at a time.

B. SPRAYER

The spray (B) applicator is NOT child-resistant. If you have small children, keep the original child-resistant cap and place it back on the bottle after each use.

1. Insert the spray applicator into the bottle and twist on firmly.

2. Next, holding the bottle upright, pump the spray attachment six (6) times to get one full dose (1 mL). Be careful not to inhale the mist.

JUL 30 1999

Store at room temperature 59°-86°F (15°-30°C). Keep tightly closed.

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ALLEGAN, MI 49010 U.S.A.

496059 10/98

IMPORTANT INFORMATION ABOUT

Minoxidil
Topical Solution, 2%

FOR MEN

Hair Regrowth Treatment

Minoxidil
Topical Solution, 2%

FOR MEN

Important information about – minoxidil topical solution, 2%

- Hair regrowth treatment
- Previously available only by prescription

Minoxidil containing topical products are the only products available without a prescription that are medically proven effective to help regrow hair.

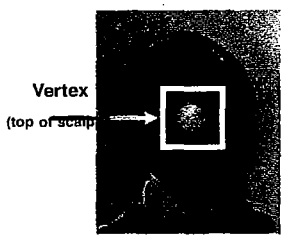
- Please read this booklet carefully. It will help you understand how to use this product and what to expect from its use. If you have any questions after reading this booklet, or anytime while using this product, you should ask your doctor or pharmacist.

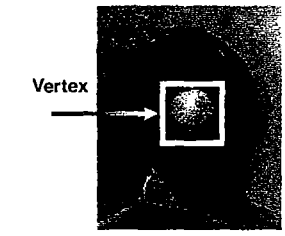
What is Minoxidil Topical Solution, 2%?
It is a colorless liquid medication for use only on the scalp to help regrow hair.

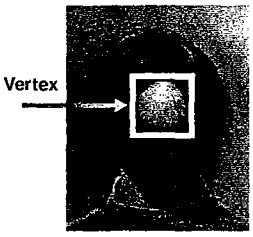
Who may use this product?
This product may be appropriate for you if you are an adult who is at least 18 years old and experiencing gradually thinning hair or gradual hair loss on the top of the head. The common hereditary thinning or hair loss process begins slowly and may become noticeable only after years of gradual loss.

This product is for men with hair loss or thinning that begins at the top of the scalp (vertex) as shown below. Frontal hair growth has not been demonstrated in clinical trials. This product is more likely to regrow hair in men with hair loss in the range shown below. If men have more hair loss than shown, this product may not work.

Many of those experiencing hair loss have other family members with gradual thinning hair or hair loss. **If there is no family history of gradual thinning hair or gradual hair loss, or hair loss is patchy, talk to your doctor.**







Who should NOT use this product?
This product will not prevent or improve hair loss which may occur with the use of some prescription and non-prescription medications, certain severe nutritional problems (very low body iron; excessive vitamin A intake), low thyroid states (hypothyroidism), chemotherapy, or diseases which cause scarring of the scalp. Also, this product will not improve hair loss due to:

- damage from the use of hair care products which cause scarring or deep burns of the scalp.
- hair grooming methods such as cornrowing or ponytails which require pulling of the hair tightly back from the scalp.

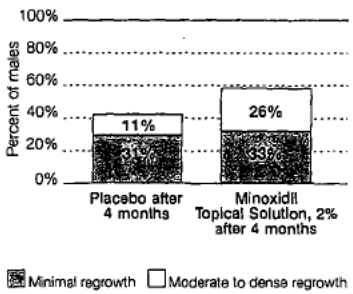
You should ask your doctor if you are unsure of the cause of your hair loss.

Will this product work for me?
The amount of hair regrowth is different for each person. Not everyone will respond to this product. The response to this product cannot be predicted. No one will be able to grow back all their hair.

You may respond better if you have been losing your hair for a short period of time or have little initial hair loss.

In clinical studies of mostly white men aged 18-49 years with moderate degrees of hair loss, the following responses to topical minoxidil were reported:

Minoxidil Response in Men
Percent reporting hair regrowth



26% of men reported moderate to dense hair regrowth after using topical minoxidil for 4 months (26% had moderate to dense regrowth; 33% had minimal regrowth). This compares with 11% of men reporting hair regrowth after using the placebo, the liquid without minoxidil in it, for 4 months (11% had moderate to dense regrowth; 31% had minimal regrowth).

What Minimal, Moderate and Dense Hair Regrowth Will Mean For You

	Number of Hairs	Hair Density
Minimal	Some new hairs are seen, but not enough to cover thinning areas.	Hairs in thinning areas do not grow as closely together as hairs on the rest of the head.
Moderate	New hairs cover some or all of thinning areas.	Hairs in the thinning areas grow more closely together, but are not as close together as hairs on the rest of the head.
Dense	New hairs cover, or almost completely cover, thinning areas.	Hairs in thinning areas grow as closely together as hairs on the rest of head.

Can this product be used to prevent hair loss?
We do not know if this product will prevent hair loss.

How soon can I expect results from using this product?
Since normal hair usually grows only ½ to 1 inch per month, hair regrowth with this product also takes time. Generally new hair growth is slow. Continued use 2 times a day for at least 4 months is usually needed before you notice hair regrowth.

If you do not see hair regrowth in 12 months, stop using this product and see your doctor.

When you first begin to use this product, your hair loss may continue for up to 2 weeks. This hair loss is temporary. If you continue to lose hair after two weeks, see your doctor.

If this product is working, what will the hair look like?
At first, hair growth may be soft, downy, colorless hair. After further use, the new hair should be the same color and thickness as the other hairs on your scalp.

How long do I need to use this product?
If you respond to this product, you will need to use it 2 times a day to keep and continue the hair regrowth. Up to 12 months of use may be needed to see your best results.

What happens if I completely stop using this product? Will I keep the new hair?
Continuous use is needed to maintain hair regrowth. If you stop using this product, the normal hair loss process will start again. You will probably lose your newly regrown hair in three to four months.

What is the dosage?
You should apply a dose (1 mL) of this product directly onto the scalp in the hair loss area **TWO TIMES A DAY**; for example, once in the morning and once at night. Each bottle should last about 25-30 days, if used as directed. Please refer to the "Directions for Use" section of this booklet.

What if I miss a dose or forget to use this product?
If you miss one or two daily doses of this product, just continue with your next dose. You should not make up for missed doses.

Can I use this product more than twice a day? Will it work faster, better?
No. This product will not work faster or better if used more than two times a day. Studies have been carefully conducted to determine the correct amount of product needed to get the best results. More frequent use or larger doses have not been shown to speed up hair growth and may increase your chance of side effects.

What are the most common side effects with this product?
The most common side effects are itching and other skin irritations of the treated area of the scalp. This product contains alcohol, which would cause burning or irritation of the eyes or sensitive skin areas. If this product accidentally gets into these areas, rinse with large amounts of cool tap water. Contact your doctor if irritation persists.

What kind of shampoo should I use with this product?
If you wash your scalp before applying this product, use a mild shampoo.

Can I use hair sprays, mousses, conditioners, gels, etc.?
There is no need to change your usual hair care routine when using this product. However, you should apply this product first and wait for it to dry before applying your styling aids.

Can I have my hair colored or permed or use hair relaxers while using this product?
We have no information that these treatments change the effect of this product. However, to avoid possible scalp irritation, you should make sure all of this product has been washed off the hair and scalp before using these chemicals.

Can I apply this product and wash my hair an hour later?
No. For this product to work best, you should allow this product to remain on the scalp for about 4 hours before washing.

Can I go swimming or out in the rain?
Yes, as long as you use good judgement. Avoid washing off this product. If possible, apply this product to a dry scalp after swimming, or wait about 4 hours after application before going swimming. Do not let your scalp get wet from the rain after applying this product.

Can this product produce unwanted hair growth?
Unwanted hair growth elsewhere on the body has been reported. This may be due to the frequent applying of product on the areas of the skin other than the scalp.

To prevent unwanted hair growth, limit the application of this product only to the scalp.

Can I use this product for baldness or hair loss in babies and children?
No. This product must not be used to treat baldness or hair loss in babies or children.

Are there any special warnings about the use of this product?

DO NOT USE THIS PRODUCT AND SEE YOUR DOCTOR IF YOU:

- Have no family history of hair loss
- Have sudden hair loss
- Have patchy hair loss
- Do not know the reason for your hair loss

DO NOT USE THIS PRODUCT IF YOU:

- Are less than 18 years old
- Have ever had an allergic reaction to minoxidil or other ingredients in this product.

As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product.

DO NOT APPLY THIS PRODUCT ON SCALP IF THE SKIN IS:

- Red or inflamed
- Infected
- Irritated
- Painful to touch (such as severe sunburn)

STOP USING THIS PRODUCT AND SEE YOUR DOCTOR IF YOU GET:

- Chest pain
- Rapid heartbeat
- Faintness and/or dizziness
- Sudden, unexplained weight gain
- Swollen hands or feet
- Redness or irritation on treated areas of your scalp

What factors may increase the risk of serious side effects with this product?
This product should be applied only to the scalp. The risk of side effects may be greater when it is applied to other parts of the body.

Directions for Use
Apply one mL 2 times a day directly onto the scalp in the hair loss area. Do not use more. Each bottle should last about 25-30 days, if used as directed. Use a mild shampoo if you wash your scalp before applying this product.

Each applicator contains one dose of medicine. It is not necessary to use fingertips when applying this product. However, if you use your hands, wash them afterwards.

Do not take this product by mouth. **Keep this and all drugs out of the reach of children. In case of accidental ingestion, seek professional assistance or contact a Poison Control Center immediately.**

If you have any other questions, ask your pharmacist.

Final Printed Labeling
ANDA 75-357
Minoxidil Topical Solution, 2%
For Men
Label

Directions: Apply one mL 2 times a day directly onto the scalp in the hair loss area. Using more, or more often will not improve results.
Warnings:
Do not use if:
- you have no family history of hair loss.
- hair loss is sudden and/or patchy.
- scalp is red, inflamed, infected, irritated or painful.
- you do not know the reason for your hair loss.
- you are under 18 years of age. Do not use on babies and children.
- you use other topical prescription products on the scalp.

Stop use and see a doctor if you get:
- chest pain, rapid heartbeat, faintness, or dizziness.
- sudden, unexplained weight gain.
- swollen hands or feet.
- redness or irritation.

Avoid eye contact. In case of accidental contact, rinse with large amounts of cool tap water.
Keep this and all drugs out of the reach of children. In case of accidental ingestion, seek professional advice or contact a Poison Control Center immediately.
As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product. Do not use if hair loss is associated with childbirth.
See carton or enclosed booklet for additional information.
Each mL contains:
Minoxidil 2% w/v. Also alcohol, 60% v/v, propylene glycol, and purified water.

Minoxidil
Topical Solution, 2%
Hair Regrowth Treatment

JUL 30 1999

APPROVED

FOR MEN

Store at room temperature 59°-86°F (15°-30°C). Keep tightly closed.

MANUFACTURED BY
PERRIGO®
ALLEGAN, MI 49010 U.S.A.

Do Not Use If You Are Under 18 Years Of Age.
External Use Only

60mL (2 FL OZ)

L 819 16 FA F

{Lot number and expiration date will appear on label.}

Final Printed Labeling
ANDA 75-357
Minoxidil Topical Solution, 2%
For Men
Carton

Minoxidil Topical Solution, 2%
FOR MEN

ACTIVE INGREDIENT: Minoxidil 2% w/v

PURPOSE: Hair regrowth treatment.

USE:
- To regrow hair on the scalp.
- It takes time to regrow hair. You may need to use this product daily for at least 4 months before you see results.
- The amount of hair regrowth is different for each person. This product will not work for everyone.
- In clinical studies of mostly white men aged 18-49 years with moderate degrees of hair loss, the following response to minoxidil 2% topical solution was reported: 26% of men reported moderate to dense hair regrowth after 4 months (26% had moderate to dense regrowth; 33% had minimal regrowth). This compares with 11% of men reporting hair regrowth after using the placebo, the liquid without minoxidil in it, for 4 months (11% had moderate to dense regrowth; 31% had minimal regrowth).
  If your degree of hair loss is more than that shown on the side of this carton, this product may not work.
- Continued use is necessary to increase and keep your hair regrowth or hair loss will begin again. If you do not see hair regrowth in 12 months, stop using and see your doctor.

DIRECTIONS: FOR EXTERNAL USE ONLY. Apply one mL 2 times a day directly onto the scalp in the hair loss area. Using more or more often will not improve results. Do not apply on other parts of the body.

WARNINGS: ***Do not use if:***
- you have no family history of hair loss.
- hair loss is sudden and/or patchy.
- scalp is red, inflamed, infected, irritated or painful.
- you do not know the reason for your hair loss.
- you are under 18 years of age. Do not use on babies and children.
- you use other topical prescription products on the scalp.

Stop use and see a doctor if you get:
- chest pain, rapid heartbeat, faintness, or dizziness.
- sudden unexplained weight gain.
- swollen hands or feet.
- redness or irritation.

READ THE LABEL

Avoid contact with eyes. In case of accidental contact, rinse with large amounts of cool tap water. As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product. Do not use if your hair loss is associated with childbirth. Keep this and all drugs out of the reach of children. In case of accidental ingestion, seek professional assistance or contact a Poison Control Center immediately.

Before use, read all label information.

Keep the carton. It contains important information.

381916FAA

JUL 30 1999

INACTIVE INGREDIENTS: Alcohol, 60% v/v, propylene glycol, and purified water.

CONTENTS:
- One 60 mL (2 FL OZ) bottle of Minoxidil Topical Solution, 2% (lasts about 25-30 days).
- Two applicators, child-resistant dropper and sprayer (not child-resistant).
- Information booklet for men.

*Rogaine® is a registered trademark of Pharmacia & Upjohn Company.

Store at room temperature 59°-86°F (15°-30°C). Keep tightly closed.

MANUFACTURED BY
PERRIGO®
ALLEGAN, MI 49010 U.S.A.

Minoxidil
Topical Solution, 2%
Hair Regrowth Treatment
FOR MEN

(Read enclosed booklet before use)
60mL (2 FL OZ)

Minoxidil
Topical Solution, 2%
Hair Regrowth Treatment

FOR MEN

Medically Proven to Help Regrow Hair

Same as Former Prescription Strength

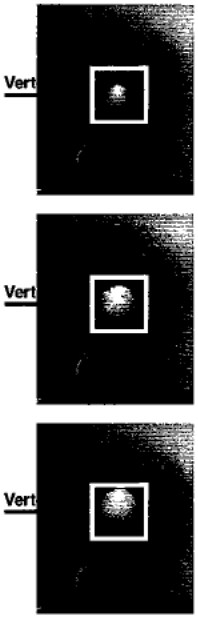
Compare to Active Ingredient of Rogaine® FOR MEN

0 00000 00000 0

3 819 16 FA A

(b) (4)

This product is for men who have a general thinning of hair on the top of the scalp (vertex) as shown. This product has been shown to regrow hair in men with the following degrees of thinning hair or hair loss.

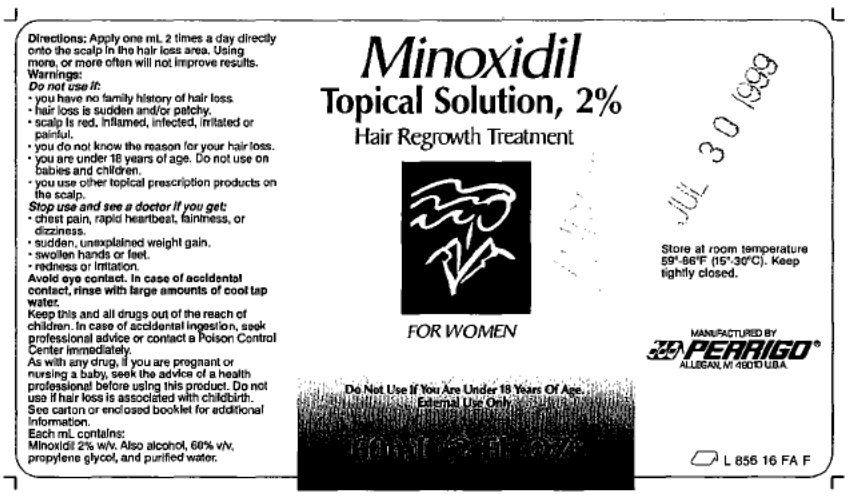


If men have more hair loss than shown above, this product may not work.

{Lot number and expiration date will appear on carton.}

8.1

Final Printed Labeling
ANDA 75-357
Minoxidil Topical Solution, 2%
For Women
Label



{Lot number and expiration date will appear on label.}

(b) (4)

Minoxidil Topical Solution, 2%
FOR WOMEN

ACTIVE INGREDIENT: Minoxidil 2% w/v

PURPOSE: Hair regrowth treatment.

USE:
- To regrow hair on the scalp.
- It takes time to regrow hair. You may need to use this product daily for at least 4 months before you see results.
- The amount of hair regrowth is different for each person. This product will not work for everyone.
- In clinical studies of mostly white women aged 18-45 years with mild to moderate degrees of hair loss, the following response to minoxidil 2% topical solution was reported: 19% of women reported moderate hair regrowth after 8 months (19% had moderate regrowth; 40% had minimal regrowth). This compares with 7% of women reporting moderate hair regrowth after using the placebo, the liquid without minoxidil in it, for 8 months (7% had moderate regrowth; 33% had minimal regrowth).
  If your degree of hair loss is more than that shown on the side of this carton, this product may not work.
- Continued use is necessary to increase and keep your hair regrowth or hair loss will begin again. If you do not see hair regrowth in 8 months, stop using and see your doctor.

DIRECTIONS: FOR EXTERNAL USE ONLY. Apply one mL 2 times a day directly onto the scalp in the hair loss area. Using more or more often will not improve results. Do not apply on other parts of the body.

WARNINGS: ***Do not use if:***
- you have no family history of hair loss.
- hair loss is sudden and/or patchy.
- scalp is red, inflamed, infected, irritated or painful.
- you do not know the reason for your hair loss.
- you are under 18 years of age. Do not use on babies and children.
- you use other topical prescription products on the scalp.

Stop use and see a doctor if you get:
- chest pain, rapid heartbeat, faintness, or dizziness.
- sudden unexplained weight gain.
- swollen hands or feet.
- redness or irritation.

READ THE LABEL

Avoid contact with eyes. In case of accidental contact, rinse with large amounts of cool tap water. As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product. Do not use if your hair loss is associated with childbirth. Keep this and all drugs out of the reach of children. In case of accidental ingestion, seek professional assistance or contact a Poison Control Center immediately.

Before use, read all label information.

Keep the carton. It contains important information.

385616FAA

INACTIVE INGREDIENTS: Alcohol, 60% v/v, propylene glycol, and purified water.

CONTENTS:
- One 60 mL (2 FL OZ) bottle of Minoxidil Topical Solution, 2% (lasts about 25-30 days).
- Extender spray applicator (not child-resistant).
- Information booklet for women.

*Rogaine® is a registered trademark of Pharmacia & Upjohn Company.

Store at room temperature 59°-86°F (15°-30°C). Keep tightly closed.

MANUFACTURED BY
PERRIGO®
ALLEGAN, MI 49010 U.S.A.

Minoxidil
Topical Solution, 2%
Hair Regrowth Treatment
FOR WOMEN

(Read enclosed booklet before use)

60mL (2 FL OZ)

Minoxidil
Topical Solution, 2%
Hair Regrowth Treatment

FOR WOMEN

Medically Proven to Help Regrow Hair

Same as Former Prescription Strength

Compare to Active Ingredient of Rogaine® Extra Strength

0 00000 00000 0

{Lot number and expiration date will appear on carton.}

3 856 16 FA A

This product is for women who have a general thinning of hair on the top of the scalp as shown. This product has been shown to regrow hair in women with the following degrees of thinning hair or hair loss.

If women have more hair loss than shown above, this product may not work.

Do not use if you have patchy hair loss as shown below.

120

Final Printed Labeling
ANDA 75-357
Minoxidil Topical Solution, 2%
For Women
Carton

STOP USING THIS PRODUCT AND SEE YOUR DOCTOR IF YOU GET:

- Chest pain
- Rapid heartbeat
- Faintness and/or dizziness
- Sudden, unexplained weight gain
- Swollen hands or feet
- Redness or irritation on treated areas of your scalp

What factors may increase the risk of serious side effects with this product?
This product should be applied only to the scalp. The risk of side effects may be greater when this product is applied to other parts of the body.

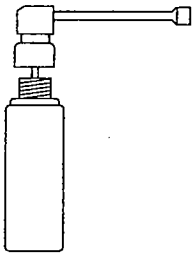
Directions for Use
Apply one mL 2 times a day directly onto the scalp in the hair loss area. Do not use more. Each bottle should last about 25-30 days, if used as directed. Use a mild shampoo if you wash your scalp before applying this product.

Each applicator contains one dose of medicine. It is not necessary to use fingertips when applying this product. However, if you use your hands, wash them afterwards.

Do not take this product by mouth. **Keep this and all drugs out of the reach of children. In case of accidental ingestion, seek professional assistance or contact a Poison Control Center immediately.**

If you have any other questions, ask your pharmacist.

Instructions for use of the Extender Spray Applicator
Hair styles and degree of hair loss can be very different for each person. We have included the extender spray to help you spray this product through the hair, directly onto the scalp.



Using the Applicator
The extender spray applicator is NOT child-resistant. If you have small children, keep the original child-resistant cap and place it back on the bottle after each use.

1. Insert the spray applicator into the bottle and twist on firmly.

2. Pull off the small spray head from the plastic tube. Fit the extender onto the plastic tube and push down firmly.

3. Pump the extender spray six (6) times to get one full dose (1 mL). Be careful not to inhale the mist.

Store at room temperature 59°-86°F (15°-30°C). Keep tightly closed.

MANUFACTURED BY
PERRIGO®
ALLEGAN, MI 49010 U.S.A.

496058 11/98

IMPORTANT INFORMATION ABOUT

Minoxidil
Topical Solution, 2%
FOR WOMEN

Hair Regrowth Treatment

Minoxidil
Topical Solution, 2%
FOR WOMEN

Important information about –
minoxidil topical solution, 2%

- Hair regrowth treatment
- Previously available only by prescription

Over 20 million American women have experienced hair thinning or hair loss, so you're not alone. Minoxidil containing topical products are the only products available without a prescription that are medically proven to help regrow hair.

Please read this booklet carefully. It will help you understand how to use this product and what to expect from its use. If you have any questions after reading this booklet, or anytime while using this product, you should ask your doctor or pharmacist.

What is Minoxidil Topical Solution, 2%?
It is a colorless liquid medication for use only on the top of the scalp to help regrow hair.

Who may use this product?
This product may be appropriate for you if you are an adult who is at least 18 years old and experiencing gradually thinning hair or gradual hair loss on the top of the head. The common hereditary thinning or hair loss process begins slowly and may become noticeable only after years of gradual loss.

This product is for general thinning of hair on the top of the scalp as shown below. This product has been shown to regrow hair in women with the degrees of hair loss shown. If women have more hair loss than shown, this product may not work.

Many of those experiencing hair loss have other family members with gradual thinning hair or hair loss. **If there is no family history of gradual thinning or gradual hair loss, or hair loss is patchy, talk to your doctor.**

Who should NOT use this product?
This product will not prevent or improve hair loss related to pregnancy, the use of some prescription and non-prescription medications, certain severe nutritional problems (very low body iron; excessive vitamin A intake), the recently discontinued use of birth control pills, low thyroid states (hypothyroidism), chemotherapy, or diseases which cause scarring of the scalp. Also, this product will not improve hair loss due to:

- damage from the use of hair care products which cause scarring or deep burns of the scalp.
- hair grooming methods such as cornrowing or ponytails which require pulling of the hair tightly back from the scalp.

Do not use this product if hair loss is patchy as shown below.

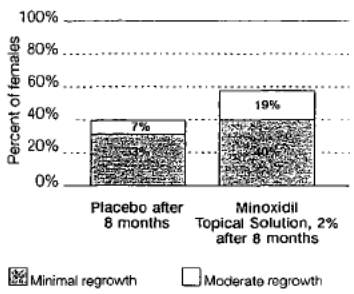
You should ask your doctor if you are unsure of the cause of your hair loss.

Will this product work for me?
The amount of hair regrowth is different for each person. Not everyone will respond to this product. The response to this product cannot be predicted. No one will be able to grow back all their hair.

In clinical studies of mostly white women aged 18-45 years with mild to moderate degrees of hair loss, the following responses to topical minoxidil were reported:

19% of women reported moderate hair regrowth after using topical minoxidil for 8 months (19% had moderate regrowth; 40% had minimal regrowth). This compares with 7% of women reporting moderate hair regrowth after using the placebo, the liquid without minoxidil in it, for 8 months (7% had moderate regrowth; 33% had minimal regrowth).

Female Response to Minoxidil
Percent reporting hair regrowth



What Minimal, Moderate and Dense Hair Regrowth Will Mean For You

	Number of Hairs	Hair Density
Minimal	Some new hairs are seen, but not enough to cover thinning areas.	Hairs in thinning areas do not grow as closely together as hairs on the rest of the head.
Moderate	New hairs cover some or all of thinning areas.	Hairs in the thinning areas grow more closely together, but are not as close together as hairs on the rest of the head.
Dense	New hairs cover, or almost completely cover, thinning areas.	Hairs in thinning areas grow as closely together as hairs on the rest of head.

Can this product be used to prevent hair loss?
We do not know if this product will prevent hair loss.

How soon can I expect results from using this product?
Since normal hair usually grows only ½ to 1 inch per month, hair regrowth with this product also takes time. Generally new hair growth is slow. Continued use of 2 times a day for at least 4 months is usually needed before you notice hair regrowth.

If you do not see hair regrowth in 8 months, stop using this product and see your doctor.

When you first begin to use this product, your hair loss may continue for up to 2 weeks. This hair loss is temporary. If you continue to lose hair after two weeks, see your doctor.

If this product is working, what will the hair look like?
At first, hair growth may be soft, downy, colorless hair. After further use, the new hair should be the same color and thickness as the other hairs on your scalp.

How long do I need to use this product?
If you respond to this product, you will need to use it 2 times a day to keep and continue the hair regrowth. Up to 8 months of usage may be needed to see your best results.

What happens if I completely stop using this product? Will I keep the new hair?
Continuous use is needed to maintain hair regrowth. If you stop using this product, the normal hair loss process will start again. You will probably lose your newly regrown hair in three to four months.

What is the dosage?
You should apply a dose (1 mL) of this product directly onto the scalp in the hair loss area **TWO TIMES A DAY**; for example, once in the morning and once at night. Each bottle should last about 25-30 days, if used as directed. Please refer to the "Directions for Use" section of this booklet.

What if I miss a dose or forget to use this product?
If you miss one or two daily doses of this product, just continue with your next dose. You should not make up for missed doses.

Can I use this product more than two times a day? Will it work faster, better?
No. This product will not work faster or better if used more than two times a day. Studies have been carefully conducted to determine the correct amount of product needed to get the best results. More frequent use or larger doses have not been shown to speed up hair regrowth and may increase your chance of side effects.

What are the most common side effects with this product?
The most common side effects are itching and other skin irritations of the treated area of the scalp. This product contains alcohol, which would cause burning or irritation of the eyes or sensitive skin areas. If this product accidentally gets into these areas, rinse with large amounts of cool tap water. Contact your doctor if irritation persists.

What kind of shampoo should I use with this product?
If you wash your scalp before applying this product, use a mild shampoo.

Can I use hair sprays, mousses, conditioners, gels, etc.?
There is no reason to change your usual hair care routine when using this product. However, you should apply this product first and wait for it to dry before applying your styling aids.

Can I have my hair colored or permed or use hair relaxers while using this product?
We have no information that these treatments change the effect of this product. However, to avoid possible scalp irritation, you should make sure all of this product has been washed off the hair and scalp before using these chemicals.

Can I apply this product and wash my hair an hour later?
No. For this product to work best, you should allow this product to remain on the scalp for about 4 hours before washing.

Can I go swimming or out in the rain?
Yes, as long as you use good judgement. Avoid washing off this product. If possible, apply this product to a dry scalp after swimming, or wait about 4 hours after application before going swimming. Do not let your scalp get wet from the rain after applying this product.

Can this product produce unwanted hair growth?
Unwanted hair growth elsewhere on the body has been reported. This may be due to the frequent applying of product on the areas of the skin other than the scalp.

To prevent unwanted hair growth, limit the application of this product only to the scalp.

Can I use this product for baldness or hair loss in babies and children?
No. This product must not be used to treat baldness or hair loss in babies or children.

Are there any special warnings about the use of this product?

DO NOT USE THIS PRODUCT AND SEE YOUR DOCTOR IF YOU:

- Have no family history of hair loss
- Have sudden hair loss
- Have patchy hair loss
- Do not know the reason for your hair loss

DO NOT USE THIS PRODUCT IF YOU:

- Are less than 18 years old
- Have ever had an allergic reaction to minoxidil or other ingredients in this product
- Have normal hair loss associated with childbirth

As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product.

DO NOT APPLY THIS PRODUCT ON SCALP IF THE SKIN IS:

- Red or inflamed
- Infected
- Irritated
- Painful to touch (such as severe sunburn)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 075357

LABELING REVIEWS

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 75-357 Date of Submission: April 13, 1998

Applicant's Name: L. Perrigo Company

Established Name: Minoxidil Topical Solution, 2%

Labeling Deficiencies:

1. GENERAL COMMENTS:

   a. Revise the established name and strength to appear as "Minoxidil Topical Solution, 2%".

   b. Include the following storage recommendations on all labels and labeling:

      Store at room temperature between 59°-86°F (15°-30°C). Keep tightly closed.

2. CONTAINER (60 mL for Men and Women)

   See GENERAL COMMENTS.

3. CARTON

   a. Male (60 mL) - See GENERAL COMMENTS.

   b. Female (60 mL)

      i. See GENERAL COMMENTS.

      ii. Revise the second bullet of the "CONTENTS" statement to read, "Extender spray applicator (not child resistant)" to be in accord with Rogaine's labeling.

4. PATIENT BOOKLET

   For Men and Women

   a. See GENERAL COMMENTS.

b. Directions for Use

Revise the ultimate paragraph to read, ...ask your pharmacist.

For Women

c. Instructions for use of Applicators

i. Revise section heading to read, Instruction for use of the Extender Spray Applicator to be in accord with Rogaine's labeling.

ii. Revise this section to be the same as Rogaine's.

Please revise your labels and labeling, as instructed above, and submit in final print.

Please note that the Agency reserves the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

John D. Grace for

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23		x	
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?	x		
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			x
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?	x		
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	

Labeling (continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?		x	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		x	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			x
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		x	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

NOTES/QUESTIONS TO THE CHEMIST:

1. Although [redacted] (b) (4) in the product for women (the [redacted] (b) (4) extender spray), [redacted] (b) (4) the extender spray applicator is [redacted] (b) (4). Perrigo is trying to [redacted] (b) (4), but they have been asked to revise their labeling to be in accord with that of the RLD. Therefore, no separate reference to the [redacted] (b) (4) should be made in their labeling.

2. The labeling states that this product contains 60% (v/v) alcohol. Please verify that this is accurate.

FOR THE RECORD:

1. Labeling review based on Upjohn's labeling for Rogaine® approved February 9, 1996, for OTC use; acknowledged and retained May 10, 1996.

2. Packaging
Rogaine packages its product in 1x60 mL, 2x60 mL, and 3x60 mL bottles.

The applicant is only proposing the 1x60 mL package size for both the male and female. The proposed bottles are HDPE with CRC for the male dropper, and non-CRC for the male and female sprayer.

3. Labeling
Perrigo made a lot of editorial changes throughout their labeling. In discussing the issue with John Grace, he did not see a problem with the changes.

Perrigo also changed the [redacted] (b) (4) the established name and strength, [redacted] (b) (4)" instead of "Minoxidil Topical Solution, 2%". Although John did not see a problem with this, the preferred format was mentioned to them.

Even though Rogaine [redacted] (b) (4) the extender spray applicator is [redacted] (b) (4). Perrigo mentions [redacted] (b) (4) and have been asked to revise their labeling to reflect that of the RLD.

4. Inactive ingredients
There appear to be no discrepancies between the labeling and the Components and Composition statements.

5. USP Issues
The applicant has been asked to include "Keep tightly closed" with their storage recommendations.

"Minoxidil Topical Solution" has been proposed in the PF (Volume 23, Number 5, page 4658).

6. Bio Issues - Waiver granted July 20, 1998.

7. Patents/Exclusivities - None pending

Date of Review:
July 24, 1998

Date of Submission:
April 13, 1998

Primary Reviewer:

Date:
8/3/98

Team Leader:

Date:
8/4/98

cc:
ANDA: 75-357
DUP/DIVISION FILE
HFD-613/LGolson/JGrace (no cc)
ldg/7/24/98/X:\NEW\FIRMSNZ\PERRIGO\LTRS&REV\75357NA1.L
Review

APPROVAL SUMMARY

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 75-357 Date of Submission: February 18, 1999 (Amendment)

Applicant's Name: L. Perrigo Company

Established Name: Minoxidil Topical Solution, 2%

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes

Container Labels: (60 mL for Men and Women)
Satisfactory as of February 18, 1999, submission

Carton Labeling: (1 x 60 mL for Men and Women)
Satisfactory as of February 18, 1999, submission

Patient Package Insert Labeling:
Satisfactory as of February 18, 1999, submission

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Rogaine Topical Solution, 2%

NDA Number: 19-501

NDA Drug Name: Minoxidil Topical Solution, 2%

NDA Firm: The Upjohn Company

Date of Approval of NDA Insert and supplement #012: February 9, 1996; acknowledged and retained May 10, 1996

Has this been verified by the MIS system for the NDA? Yes

Was this approval based upon an OGD labeling guidance? No

Basis of Approval for the Container Labels: Side-by-side

comparison

Basis of Approval for the Carton Labeling: Side-by-side comparison

---

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N A
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23		x	
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?	x		
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			x
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?	x		
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?			x

Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
Labeling (continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?		x	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		x	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			x
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		x	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	

Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

FOR THE RECORD:

1. Labeling review based on Upjohn's labeling for Rogaine® approved February 9, 1996, for OTC use; acknowledged and retained May 10, 1996.

2. Packaging
   Rogaine packages its product in 1x60 mL, 2x60 mL, and 3x60 mL bottles.

   The applicant is only proposing the 1x60 mL package size for both the male and female. The proposed bottles are HDPE with CRC for the male dropper, and non-CRC for the male and female sprayer.

3. Labeling
   Perrigo made a lot of editorial changes throughout their labeling. In discussing the issue with John Grace, he did not see a problem with the changes.

4. Inactive ingredients
   There appear to be no discrepancies between the labeling and the Components and Composition statements.

5. USP Issues
   "Minoxidil Topical Solution" has been proposed in the PF (Volume 23, Number 5, page 4658).

6. Bio Issues - Waiver granted July 20, 1998.

7. Patents/Exclusivities - None pending

Date of Review:
March 12, 1999

Date of Submission:
February 18, 1999 (Amendment)

Primary Reviewer:
Ted Dolson

Date:
3/13/99

Team Leader:
John J Grace

Date:
3/15/1999

Concur: Wellspeak 3/15/99

cc:

ANDA: 75-357
DUP/DIVISION FILE
HFD-613/LGolson/JGrace (no cc)
ldg/3/12/99/X:\NEW\FIRMSNZ\PERRIGO\LTRS&REV\75357AP.L
Review

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 075357

CHEMISTRY REVIEWS

1. CHEMISTRY REVIEW NO. 1

2. ANDA # 75-357

3. NAME AND ADDRESS OF APPLICANT

L. Perrigo Company
112 Water Street
Allegan, MI 49010

4. LEGAL BASIS FOR SUBMISSION

"In the opinion and to the best knowledge of L. Perrigo Company there are no patents that claim the listed drug product referred to in this application or that claim a use of the listed drug product." There is no market exclusivity information on file for Rogaine minoxidil 2% topical solution.

5. SUPPLEMENT(s)

N/A

6. PROPRIETARY NAME

None

7. NONPROPRIETARY NAME

Minoxidil Solution

8. SUPPLEMENT(s) PROVIDE(s) FOR:

N/A

9. AMENDMENTS AND OTHER DATES:

Original submission April 13, 1998

10. PHARMACOLOGICAL CATEGORY

Hair growth

11. Rx or OTC

OTC

12. RELATED IND/NDA/DMF(s)

DMF # Manufacturer Component

[redacted] (b) (4)

13. DOSAGE FORM

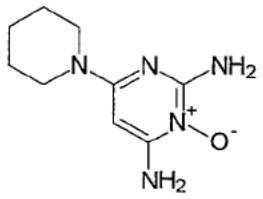
Solution

14. POTENCY

2%

15. CHEMICAL NAME AND STRUCTURE

2,4-Pyrimidinediamine, 6-(1-piperidinyl)-, 3-oxide.
$C_9H_{15}N_5O$.



16. RECORDS AND REPORTS

None

17. COMMENTS

The application was found deficient.

18. CONCLUSIONS AND RECOMMENDATIONS

The application is not approvable.

19. REVIEWER: DATE COMPLETED:

Kathy P. Woodland August 31, 1998

Following this page, 11 pages withheld in full (b)(4)

38. Chemistry Comments to be Provided to the Applicant

ANDA: 75-357 APPLICANT: L. Perrigo Company

DRUG PRODUCT: Minoxidil Topical Solution 2%

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. (b) (4)

2.

3.

4. Regarding the packaging compatibility study:

a. (b) (4)

b.

c.

5. (b) (4)

6.

7. [redacted] (b) (4)

8. Please revise the stability tests and specifications to include:

   a. [redacted] (b) (4)

   b.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response that:

   1. The firms referenced in your application must be in compliance with CGMP at the time of approval.

   2. A Methods Validation for the Drug Product will be performed by the FDA laboratory. Please submit samples promptly when requested.

Sincerely yours,

10/8/96

for Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-357
ANDA DUP
Division File
Field Copy

Endorsements: (Draft and Final with Dates):

HFD-627/K.Woodland/9/18/98 Woodland 9/22/98
HFD-627/P.Schwartz, Ph.D./9/18/98 23/98
HFD-617/J.Buccine, PM/9/18/98 JB 9/24/98
X:\NEW\FIRMSNZ\PERRIGO\LTRS&REV\75357.RV1
F/T by: gp/9/22/98

CHEMISTRY REVIEW - NOT APPROVABLE - MINOR

1. CHEMISTRY REVIEW NO. 2

2. ANDA # 75-357

3. NAME AND ADDRESS OF APPLICANT

L. Perrigo Company
112 Water Street
Allegan, MI 49010

4. LEGAL BASIS FOR SUBMISSION

"In the opinion and to the best knowledge of L. Perrigo Company there are no patents that claim the listed drug product referred to in this application or that claim a use of the listed drug product." There is no market exclusivity information on file for Rogaine minoxidil 2% topical solution.

5. SUPPLEMENT(s)

N/A

6. PROPRIETARY NAME

None

7. NONPROPRIETARY NAME

Minoxidil Solution

8. SUPPLEMENT(s) PROVIDE(s) FOR:

N/A

9. AMENDMENTS AND OTHER DATES:

Original submission	April 13, 1998
Amendment	February 18, 1999
Amendment	May 19, 1999
Amendment	July 9, 1999
Amendment	July 27, 1999

10. PHARMACOLOGICAL CATEGORY
Hair growth

11. Rx or OTC
OTC

12. RELATED IND/NDA/DMF(s)

DMF #	Manufacturer	Component
(b) (4)		

(b) (4)

13. DOSAGE FORM

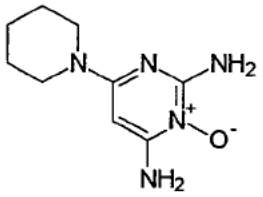
Solution

14. POTENCY

2%

15. CHEMICAL NAME AND STRUCTURE

2,4-Pyrimidinediamine, 6-(1-piperidinyl)-, 3-oxide.
$C_9H_{15}N_5O$.



16. RECORDS AND REPORTS

None

17. COMMENTS

None.

18. CONCLUSIONS AND RECOMMENDATIONS

The application is approvable.

19. REVIEWER: Kathy P. Woodland

DATE COMPLETED: July 13, 1999

Following this page, 12 pages withheld in full (b)(4)

Comments:

Comments:

ACTION CODES: (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").

Page -- of -- . Kathy P. Woodland (Reviewer) Kathy P. Woodland (Signature) 7/13/99 (Date)

cc: ANDA 75-357
ANDA DUP
Division File
Field Copy

Endorsements: (Draft and Final with Dates):

HFD-627/K.Woodland/ KWoodland 7/13/99
HFD-627/P.Schwartz, Ph.D./ PS 7/13/99
V:\FIRMSNZ\PERRIGO\LTRS&REV\75357RV2.DOC
F/T by:

CHEMISTRY REVIEW - APPROVABLE

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 075357

BIOEQUIVALENCE REVIEWS

Minoxidil Topical Solution
2%
ANDA #75-357
Reviewer: Jahnavi S. Kharidia
X:\new\firmsnz\perrigo\75357w.498

L. Perrigo Company
112 Water Street
Submission Date:
April 13, 1998

Review of a Waiver Request

Objective:

The firm has requested a waiver of *in vivo* bioavailability study requirements for its drug product, Minoxidil Topical Solution, 2% for both men and women. The reference drug product is Rogaine® Topical Solution for men and Rogaine® Topical Solution for women manufactured by Upjohn.

Formulation: (Not to be released under FOI)

The test and reference formulations are compared in Table 1.

Table 1. Test and Reference Formulations

Ingredient	Test Product#	Rogaine®#
Minoxidil USP	2.0% w/v	2.0% w/v
Alcohol USP	60.0 % v/v	60.0 % v/v
Propylene Glycol USP Water	(b) (4)	

The men's and women's product do not differ in formula.
There is difference in the labeling for men's and women's product (vol 1.1, pg. 12)

Comments

1. The test product and the reference listed drug are both topical solutions containing the same active ingredient in the same concentration and dosage form.

2. The test product contains no inactive ingredient or other change in the formulation from the reference listed drug that may significantly affect potency of active ingredient.

3. A waiver is granted.

Recommendation

The Division of Bioequivalence agrees that the information submitted by L. Perrigo Company on its drug product, Minoxidil Topical Solution, 2% falls under 21 CFR section 320.22(b)(3) of the Bioavailability/Bioequivalence Regulations. The waiver of *in vivo* bioequivalence study for the drug is granted. From the Bioequivalence point of view, the Division of Bioequivalence deems Minoxidil Topical Solution, 2% manufactured by L. Perrigo Pharmaceuticals to be bioequivalent to the Upjohn's Rogaine® Topical Solution, 2%.

Jahnavi S. Kharidia
Jahnavi S. Kharidia
Division of Bioequivalence
Review Branch III

RD INITIALLED BY BDAVIT 7/20/98
FT INITIALLED BY BDAVIT Barbara Davit Date: 7/20/98

Concur: Dale P. Conner Date: 7/20/98
Dale P. Conner, Pharm.D.
Director
Division of Bioequivalence

cc: ANDA # 75-357 (original, duplicate), Kharidia, HFD-658, Drug File, Division File

OFFICE OF GENERIC DRUGS

DIVISION OF BIOEQUIVALENCE

ANDA # 75-357 SPONSOR : L. Perrigo Company
DRUG & DOSAGE FORM : Minoxidil Topical Solution, 2%
For men and women
STRENGTH(s) : 2.0%
TYPE OF STUDY: SD SDF MULT X OTHER

STUDY SUMMARY : N/A

Formulation is acceptable, waiver is granted

PRIMARY REVIEWER : Jahnavi S. Kharidia BRANCH :3
INITIAL : Jahnavi S. Kharidia DATE : 7/20/98

Team Leader : Barbara M. Davit . BRANCH : 3
INITIAL : Barbara M Davit DATE : 7/20/98

DIRECTOR
DIVISION OF BIOEQUIVALENCE
INITIAL : DRL DATE : 7/20/98

DIRECTOR
OFFICE OF GENERIC DRUGS
INITIAL : _____ DATE :

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA:75-357 APPLICANT: L. Perrigo

DRUG PRODUCT: Minoxidil Topical Solution

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

Dale P. Conner

Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 075357

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

RECORD OF TELEPHONE CONVERSATION

Subject: Missing Basis of Submission on form 356h.

Perrigo Co. will submit hard copy of revised 356h via Federal Express.

DATE
4/22/98

ANDA NUMBER
75-357

IND NUMBER

TELECON

INITIATED BY _ **APPLICANT/ SPONSOR** X **FDA**

MADE BY TELE. _ **IN PERSON**

PRODUCT NAME
Minoxidil Topical Solution, 2%

FIRM NAME
Perrigo Co.

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD
(b) (6)
Executive Secretary.

TELEPHONE NUMBER
(616) 673-7603

SIGNATURE
Denise Huie

ANDA 75-357

L. Perrigo Company
Attention: Brian R. Schuster
117 Water Street
Allegan, Michigan 49010

APR 27 1998

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to your correspondence dated April 22, 1998.

NAME OF DRUG: Minoxidil Topical Solution, 2%

DATE OF APPLICATION: April 13, 1998

DATE (RECEIVED) ACCEPTABLE FOR FILING: April 14, 1998

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Joseph Buccine
Project Manager
(301) 827-5848

Sincerely yours,

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-357
cc: DUP/Jacket
Division File
Field Copy
HFD-610/J.Phillips
HFD-615/M.Bennett
HFD-324/M.Lynch

Endorsements:
HFD-615/P.Rickman, Chief, RSB/ 4/27/98
HFD-615/D.Huie/PM/
HFD-629/P.Schwartz/Sup. Chem./
x:\new\firmsnz\perrigo\ltrs&rev\75357.ack
FT/mjl/4/22/98
ANDA Acknowledgment Letter!

CDER Establishment Evaluation Report for April 27, 1998

Application: **ANDA 75357/000**
Stamp: **14-APR-1998** Regulatory Due:
Applicant: **PERRIGO**
117 WATER ST
ALLEGAN, MI 49010

Priority:
Org Code: **600**
Action Goal:
District Goal: **14-JUN-1999**
Brand Name:
Established Name: **MINOXIDIL**
Generic Name:
Dosage Form: **SOL (SOLUTION)**
Strength: **2%**

FDA Contacts: **J. BUCCINE (HFD-617) 301-827-5848 , Project Manager**
P. SCHWARTZ (HFD-629) 301-827-5848 , Team Leader

Overall Recommendation:

Establishment: (b) (4)

DMF No: (b) (4)
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **SUBMITTED TO OC**
Milestone Date: **27-APR-1998**

Responsibilities: **DRUG SUBSTANCE MANUFACTURER**

Establishment: **1811666**
PERRIGO CO
117 WATER ST
ALLEGAN, MI 49010

DMF No:
AADA No:

Profile: **LIQ** OAI Status: **NONE**
Last Milestone: **SUBMITTED TO OC**
Milestone Date: **27-APR-1998**

Responsibilities: **FINISHED DOSAGE MANUFACTURER**

MINOR AMENDMENT

OCT 9 1998

ANDA 75-357

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

TO: APPLICANT: L. Perrigo Company PHONE: 616 673 8451

ATTN: Brian Schuster FAX: 616 673 7655

FROM: Joseph Buccine PROJECT MANAGER (301) 827–5848

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated April 13, 1998, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Minoxidil Topical Solution, 2%.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (5 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

Chemistry, labeling and bioequivalency comments are provided.

PMBS 10/9/98

X:\new\ogdadmin\macros\faxmin.frm

OCT 9 1998

38. Chemistry Comments to be Provided to the Applicant

ANDA: 75-357 APPLICANT: L. Perrigo Company

DRUG PRODUCT: Minoxidil Topical Solution 2%

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. (b) (4)

2.

3.

4. Regarding the packaging compatibility study:

a. (b) (4)

b.

c.

5. (b) (4)

6.

7. [redacted] (b) (4)

8. Please revise the stability tests and specifications to include:

   a. [redacted] (b) (4)

   b.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response that:

1. The firms referenced in your application must be in compliance with CGMP at the time of approval.

2. A Methods Validation for the Drug Product will be performed by the FDA laboratory. Please submit samples promptly when requested.

Sincerely yours,

S.(

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **ANDA 75357/000**
Stamp: **14-APR-1998** Regulatory Due:
Applicant: **PERRIGO**
117 WATER ST
ALLEGAN, MI 49010

Priority:
Org Code: **600**
Action Goal:
District Goal: **14-JUN-1999**
Brand Name:
Established Name: **MINOXIDIL**
Generic Name:
Dosage Form: **SOL (SOLUTION)**
Strength: **2%**

FDA Contacts: **J. BUCCINE (HFD-617) 301-827-5848 , Project Manager**
P. SCHWARTZ (HFD-629) 301-827-5848 , Team Leader

Overall Recommendation:

ACCEPTABLE on 25-MAY-1999 by M. EGAS (HFD-322) 301-594-0095
ACCEPTABLE on 12-JUN-1998 by M. EGAS (HFD-322) 301-594-0095

Establishment: (b) (4)
DMF No: (b) (4)
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **25-MAY-1999**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**
Responsibilities: **DRUG SUBSTANCE MANUFACTURER**

Establishment: **1811666**
PERRIGO CO
WATER ST/HOOKER RD/EASTERN A
ALLEGAN, MI 49010
DMF No:
AADA No:

Profile: **LIQ** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **24-MAY-1999**
Decision: **ACCEPTABLE**
Reason: **BASED ON FILE REVIEW**
Responsibilities: **FINISHED DOSAGE MANUFACTURER**

RECORD OF TELEPHONE CONVERSATION

Following tertiary review by Allan Rudman, the firm was called to provide the following information.

1. Regarding stability, there is an [redacted (b) (4)] ? Please explain.

2. We note that [redacted (b) (4)] Please explain.

The firm will provide their explanation via t-amendment.

Cc:
ANDA
T-con Binder

X:\NEW\FIRMSNZ\PERRIGO\TELECONS\75357.002

DATE
6/18/99

APPLICATION NUMBER
75-357

TELECON

FDA PARTICIPANTS
Kathy Woodland
Joe Buccine

PRODUCT NAME
Minoxidil 2%

FIRM NAME
Perrigo

FIRM PARTICIPANTS
Brian Schuster
Shelly Meecham
[redacted (b) (6)]
Perry Truit

TELEPHONE NUMBER
616-673-9745

SIGNATURE

ANDA APPROVAL SUMMARY

ANDA:	CHEMIST:	DATE:
75-357	Kathy P. Woodland	May 21, 1999

DRUG PRODUCT:
Minoxidil Solution

FIRM:
L.. Perrigo Company

DOSAGE FORM:	STRENGTH:
Solution (Topical)	2%

cGMP:
Acceptable 5/25/99

BIO:
Waiver granted 7/20/98, J. Kharidia

VALIDATION - *(Description of dosage form same as firm's):*
Acceptable by Detroit District , 3/16/99 USP product (supp. 9)

STABILITY:
Containers in the stability studies are identical to those in the container section.

LABELING:
Approved by L. Golson, 3/13/99

STERILIZATION VALIDATION *(If applicable)*:
N/A

SIZE OF BIO BATCH *(Firm's source of NDS ok?)*:
Waiver granted.

SIZE OF STABILITY BATCHES *(If different from bio batch, were they Manufactured via the same process?):*
Stability batch size was (b) (4)

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME?:
The proposed production size is (b) (4) the manufacturing process is the same.

Signature of chemist:	Signature of supervisor:
Kathy P. Woodland	P S [illegible] 7/16/99

V:\FIRMSNZ\PERRIGO\LTRS&REV\75357APSUM.WOR.DOC

MINUTES OF PHONE CALL

DATE: 7/19/99

SUBJECT: ANDA 75-357

ORGANIZATION: **Perrigo**

PARTICIPANTS: Allen Rudman
Shelly Meachum 616-686-1575

Shelley clarified the meaning of the stability commitment labeled as "changes" which covered post approval (b) (4) changes. She said that all post approval changes in (b) (4) would be filed under the appropriate section of 314.70 and that the section was meant solely as a notice to that changed (b) (4) would be placed on stability.

There did not appear to be any specifications for the (b) (4) Shelley said that she would contact me tomorrow about this.

7/26/99 I contacted Shelley today and asked about the status of the commitment for the (b) (4). She informed me that the firm performed testing on the test batch and asked if that were enough. I asked her for a commitment to perform (b) (4). She said that she would have to talk to her boss, Brian Shuster, and would get back to me within a few days. I asked that she contact me ASAP with a fax commitment.

OGD APPROVAL ROUTING SUMMARY

ANDA # 75-357 Applicant L. PERRIGO CO.
Drug MINOXIDIL TOPICAL SOLN USP Strength 2%

APPROVAL ■ TENTATIVE APPROVAL □ SUPPLEMENTAL APPROVAL (NEW STRENGTH) □ OTHER □

REVIEWER:

1. Project Manager BUCCINE III
Review Support Br

DRAFT RECEIPT
Date 7/14/99
Initials JB

FINAL ACTION
Date
Initials

Application Summary:

Original Rec'd date 4-14-98
Date Acceptable for Filing "
Patent Certification (type) II
Date of Office Bio Review 7-20-98
* Methods Val. Samples Pending Yes □ No ■
30 Day Clock Start End
Commitment Rcd. from Firm Yes □ No □
First Generic Yes □ No ■

EER Status Pending □ Acceptable ■ OAI □
Date of EER Status 5-25-99
Date Patent/Exclus.expires N/A
Citizens Petition/Legal Case Yes □ No ■
(If YES, attach email from PM to Pet. Coord. notifying of pending approval)
Pediatric Exclusivity Tracking System
Date checked 7/14/99
Nothing Submitted ■
Written request issued □
Study Submitted □

* NEW USP PRODUCT (SUPP #9)

Previously reviewed and tentatively approved □ Date
Previously reviewed and CGMP def./N/A Minor issued □ Date
Comments:

2. Div. Dir./Deputy Dir.
Chemistry Div. I or II
Comments:

Date 7/27/99
Initials

Date 7/27/99
Initials

Satisfactory

3. Office Level Chem Review **(1st Generic Only)**
Chemistry Div. I or II
Comments: N/A Multiple generic approvals of this drug product. RWJ 1/30/99

Date
Initials

Date
Initials

4. Pat Beers Block
Supv., Review Support Branch
RLD = 19501

Date 7/28/99
Initials

Date 7/29/99
Initials

EER Status: Acceptable for all manufacturing sites as of 5/25/99 (from OAI

Bioequivalence sites: N/A
Clinical site:
Inspection needed: □ yes □ no
Status: □acceptable □unacceptable □ pending
Date of status:
Analytical site: N/A
Inspection needed: □ yes □ no
Status: □acceptable □unacceptable □ pending
Date of status:

Labeling Status: Acceptable for OTC. container of 60 ml. as of 3/15/99

Bioequivalence office level sign off: Bioequivalence waiver granted under 320.22(b)(3) on 7/20/99
Microbiology status: N/A
Patent Certification: NO patents or exclusivity listed for RLD
Controlled Correspondence/Cit.Pet: None
Comments: M.V. sample analyzed by Detroit District lab. on 3/16/99
However the product became a U.S.P. product on 11/15/98 (9th Supplement) ** M.V. not critical. Problems were discovered