

Active ingredient
Butenafine hydrochloride 1%...

**Purpose** .....Antifungal

Net Wt 12g (0.42 oz)

23562-00

**Uses** • cures most athlete's foot between the toes, jock itch and ringworm • relieves itching, burning, cracking, and scaling which accompany these conditions

releves nching, ourning, cracking, also scanny minor sections by Warnings
 To external use only
 To not use • on nails or scalp • in or near the mouth or the eyes • for vaginal yeast infections
 When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water.
 Stop use and ask a doctor if too much irritation occurs or gets worse.
 Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.
 Aircections

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.

Directions

- adults and children 12 years and older

- use the tip of the cap to break the seal and open the tube

- use the tip of the cap to break the seal and open the tube

- use the tip of the cap and water and dry completely before applying

- for athlete's foot between the foes: apply to affected skin between and around the toes twice a day for 1 weeks, or as directed by a doctor.

Wear well-fitting, ventilated shoes. Change shoes and socks at least once daily.

- for jock ith and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor

- wash hands after each use

- children under 12 years: ask a doctor

Store at 5° - 30°C (41° - 86°F). See crimp for lot number and expiration date

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23564-00

Net Wt 24g (0.85 oz)

Active ingredient
Butenafine hydrochloride 1%...

**Purpose** ..Antifungal

Uses
■ Cures most athlete's foot between the toes, jock itch and ringworm
■ relieves itching, burning, cracking, and scaling which accompany these conditions

Warnings For external use only

Do not use

on nails or scalp

in or near the mouth or the eyes

for vaginal yeast infections

When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water.

Stop use and ask a doctor if too much irritation occurs or gets worse.

**Keep out of reach of children.** If swallowed, get medical help or contact a Poison Control Center right away.

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.

Directions

- adults and children 12 years and older

- use the tip of the cap to break the seal and open the tube

- wash the affected skin with soap and water and dry completely before applying

- for athlete's foot between the foes: apply to affected skin between and around the toes twice a day for 1 week (morning and night), or once a day for 4 weeks, or as directed by a doctor. Wear well-fitting, ventilated shoes. Change shoes and socks at least once daily.

- for jock itch and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor

- wash hands after each use

- children under 12 years: ask a doctor

Store at 5° - 30°C (41° - 86°F). See crimp for lot number and expiration date ©2001 Distributed by Schering-Plough HealthCare Products, Inc., Memphis, TN 38151 U.S.A. All rights reserved. Made in U.S.A.



ANTIFUNGAL

Active ingredient
Butenafine hydrochloride 1%.

**Purpose** ...Antifungal

Net Wt 12g (0.42 oz)

23565-00

Uses

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right:

Directions

- adults and children 12 years and older

- use the tip of the cap to break the seal and open the tube

- wash the affected skin with spap and water and dry completely before applying

- apply once a day to affected skin for 2 weeks or as directed by a doctor

- wash hands after each use

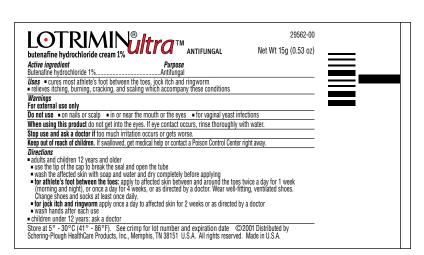
- children under 12 years: ask a doctor

Store at \$5^- > 0.0^- (At 1° - 86°F). See crimp for lot number and expiration date

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- · Relieves Itching and Burning
- \*Full Prescription Strength





Net Wt 15g (0.53 oz)



1 week twice a day or 4 weeks once a day

2901 941 Apply between and aroung

**ANTIFUNGAL** 







Wist us at www.lotrimin.com © Constributed by Schering-Plough HealthCare Products, Inc., Memphis, TV 188.U 16.A. A.D. Inghts reserved. Made in J.S.U in Made i 59229-00

**Inactive ingredients** benzyl alcohol, cetyl alcohol, diethanolamine, glycerin, glyceryl monostearate SE, polyoxyethylene (23) cetyl ether, propylene glycol dicapnylate, purfiled water, sodium benzoate, stearic acid, white petrolatum

■ do not use if seal on tube is broken or is not visible ■ store at 5° - 30°C (41° - 86°F)

Other information

- children under 12 years: ask a doctor
- uses the tip of the cap to bresk the seal and open the tube
   uses the tip of the cap to bresk the seal and once a day for 4 weeks, or as directed by a doctor. Wear well-fitting, vernitisted shoes. Change shoes and socks at least once daily.
   for 1 week (morning and night), or once a day for 4 weeks, or as directed by a doctor. Wear well-fitting, vernitisted shoes. Change shoes and socks at least once daily.
   for 1 week (morning and night), or once a day for 4 weeks, or as directed by a doctor.
  - - - - adults and children 12 years and older

**Keep out of reach of children.** If swallowed, get medical help or contact a Poison Control Center right away Stop use and ask a doctor if too much irritation occurs or gets worse

When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water. ■ in or near the mouth or the eyes

- relieves itching, burning, cracking, and scaling which accompany these conditions
- cures most athlete's foot between the foes. Effectiveness on the bottom or sides of foot is unknown.

   cures most jock itch and ingworm

Active ingredient
% t əbirolhorbyd ənitənətu

Drug Facts

**920q1u¶** IsgnutitnA .

Dutenafine hydrochloride cream 1% ULT STATE





- · Relieves Itching, **Burning** and Chafing
- Full Prescription Strength



# butenafine hydrochloride cream 1%



Net Wt 15g (0.53 oz)





wisit us at www.lotrimin.com

butenafine hydrochloride cream 1%

Wist us at www. Jotinmin.com © 2001 Distributed by Schering-Plough HealthCare Products, Inc., Memphis, TN 38151 U.S.A. All rights reserved. Made in U.S.A.

**Inactive ingredients** benzyl alcohol, celyl alcohol, diethanolamine, glycerin, glyceryl monostearate SE, polyoxyethylene (23) celyl ether, propylene glycol dicapnylate, purflied water, sodium benzoate, stearic acid, white petrolatum

- Other information

  do not use if seal on tube is broken or is not visible

  store at 5° 30°C (41° 86°F)
  - - children under 12 years: ask a doctor
- adults and children 12 years and over

  use the tip of the cap to break the seal and open the tube

  wash the affected skin with soap and water and dry completely before applying

  a wash tone a day to affected skin for 2 weeks or as directed by a doctor

  a apply once a day to affected skin for 2 weeks or as directed by a doctor

  a part of the complete standard or a search or a

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away

Stop use and ask a doctor if too much irritation occurs or gets worse

When using this product do not get into the eyes. If eye contact occurs, rinse eyes thoroughly with water Do not use  $\blacksquare$  on nails or scalp  $\blacksquare$  in or near the mouth or the eyes  $\blacksquare$  for vaginal yeast infections

For external use only **SgninnsW** 

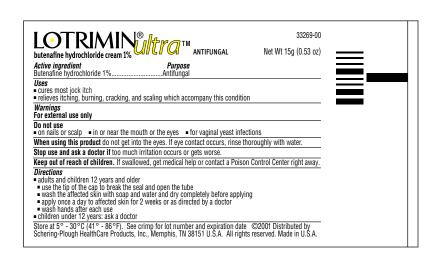
- relieves itching, burning, cracking, and scaling which accompany this condition
  - cures most jock itch

**Purpose** Antifungal **Active ingredient** Butenafine hydrochloride 1%

Drug Facts

LOTRIMIL<sup>®</sup>UÉRA





- Relieves Itching and Burning
- Full Prescription Strength



butenafine hydrochloride cream 1% **ANTIFUNGAL** 

Net Wt 30g (1.1 oz)



1 week twice a day or 4 weeks once a day

Apply between and around the toes



wisit us at www.lotrimin.com

**JADNUJITNA** butenafine hydrochloride cream 1%

00-19967 © 2001 Distributed by Schering-Plough HealthOare Products, Inc., Memphis, TN 38151 U.S.A. All rights reserved. Made in U.S.A.

**Inactive ingredients** benzyl alcohol, cetyl alcohol, diethanolamine, glycerin, glyceryl monostearate SE, polyoxyethylene (23) cetyl ether, propylene glycol dicaprylate, purfled water, sodium benzoate, stearic acid, white petrolatum

Other information = do not use if seal on tube is broken or is not visible (\* 7° - 8° 7°)

- eachurs and cnilioren 12 years and older
   wash the set be best the seal and open the tube
   wash the affected skin with soap and water and dry completely before applying
   wash the affected skin with soap and water and dry completely before applying
   for althete's foot between the loses; apply to affected skin between and around the toes fwice a day
   for lock litch and ringworm apply once a day for 4 weeks, or as directed by a doctor. Wear well iffing, venifiated shoes. Change shoes and socks at lesst once daily.

   iffing, venifiated shoes. Change shoes and socks at lesst once a daily.

   if or Jock litch and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor.

   in a day to a day to affect a skin for 2 weeks or as directed by a doctor.

   in a day to a day to affect a skin for 2 weeks or as directed by a doctor.

   in a day to a day to affect a skin for 2 weeks or as directed by a doctor.

   in a day to a day to

op use and ask a doctor if too much irritation occurs or gets worse

When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water. Do not use ■ on nails or scalp ■ in or near the mouth or the eyes ■ for vaginal yeast infections

- telleves tiching, burning, cracking, and scaling which accompany these conditions
- nost athlete's foot between the toes. Effectiveness on the bottom or sides of foot is unknown.

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	nd Facts

MINITERIAL STREET TO THE PROPERTY OF THE PROPE

OTRIMINultra



LOTRIMIN<sup>®</sup> ANTIFUNGAL butenafine hydrochloride cream 1% **Purpose** .Antifungal Active ingredient
Butenafine hydrochloride 1%

29560-00

Net Wt 30g (1.1 oz)

Uses

Uses

cures most athlete's foot between the toes, jock itch and ringworm
relieves itching, burning, cracking, and scaling which accompany these conditions

Warnings
For external use only

Do not use
on nalis or scalp
in or near the mouth or the eyes
for vaginal yeast infections

When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water.

Stop use and ask a doctor if too much irritation occurs or gets worse.

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.

Directions

Keep out of reach of children. It Swallowed, your model.

Directions

adults and children 12 years and older

use the tip of the cap to break the seal and open the tube

wash the affected skin with soap and water and dry completely before applying

for athlete's foot between the toes: apply to affected skin between and around the toes twice a day for 1 week (morning and night), or once a day for 4 weeks, or as directed by a doctor. Wear well-fitting, ventilated shoes. Change shoes and socks at least once daily.

for jock itch and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor

wash hands after each use

children under 12 years: ask a doctor

Store at 5° - 30° C (41° - 86°F). See crimp for lot number and expiration date @2001 Distributed by Schering-Plough HealthCare Products, Inc., Memphis, TN 38151 U.S.A. All rights reserved. Made in U.S.A.





# butenafine hydrochloride cream 1%

butenafine hydrochloride cream 1% ANTIFUNGAL

Net Wt 12g (0.42 oz)



1 week twice a day or 4 weeks once a day

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**ANTIFUNGAL** 

csrton recyclable

wisit us at www.lotrimin.com

butenafine hydrochloride cream 1%

S.2073-00 @ A.2.U ni absM. Devrsean zitrigin IIA. A.2.U 12186 NT , ainfimmM, and its reserved. Made in Made in M.2.U ni absM. Devrsean inghts reserved.

**Inactive ingredients** benzyl alcohol, cetyl alcohol, diethanolamine, glycerin, glyceryl monostearate SE, polyoxyethylene (23) cetyl ether, propylene glycol dicaprylate, purified water, sodium benzoate, stearic acid, white petrolatum

■ do not use if seal on tube is broken or is not visible ■ store at 5° - 30°C (41° - 86°F) Other information

- children under 12 years: ask a doctor
- for lock itch and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor wash hands affer each use
- adults and children 12 years and older adultion 12 years and older and the table and the cap to break the seal and open the tube

   wash the disclered stim with soap and waiter and dry completely before applying
   for shicle's foot between the foes: apply to affected skin between and around the toes twice a day for 1 week (morning and night), or once a day for 4 weeks, or as diest once a day for 4 weeks, or as diest once a day for 1 week once and accorded by a doctor. Wear well-filling, ventilated shoes. Change shoes and accoks a least once daily.

ceep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away. Stop use and ask a doctor if too much irritation occurs or gets worse

When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water. Do not use ■ on nails or scalp ■ in or near the mouth or the eyes ■ for vaginal yeast infections

For external use only

- Warnings
- cures most athlete's foot between the toes. Effectiveness on the bottom or sides of foot is unknown.
   cures most jock itch and ringworm
   relieves itching, burning, cracking, and scaling which accompany these conditions

Purpose Antifungal

**Active ingredient** Wr ebirochloorbyn enitsnetu

Drug Facts

LOTISIANI SUITE Dutensfine hydrochloride cream 1%

LOTRIMIN*ultra*"



## OTRIMIN<sup>®</sup> butenafine hydrochloride cream 1% **ANTIFUNGAL**

## butenafine hydrochloride cream 1% **ANTIFUNGAL**

Net Wt 12g (0.42 oz)

BAR CODE



moo.nimirtol.www ts zu tisiv carton carton



23778-00

© 2001 Distributed by Schering-Plough HealthCare Products, Inc., Memphis, TN 38151 U.S.A. All rights reserved. Made in U.S.D.

**Inactive ingredients** benzyl alcohol, cetyl alcohol, diethanolamine, glycerin, glyceryl monostearate SE, polyoxyethylene (23) cetyl ether, propylene glycol dicapnylate, purfled water, sodium benzoate, stearic acid, white petrolatum

- **Other information**do not use if seal on tube is broken or is not visible

  do not use if \$6 30°C (41° 86°F)

  - wash hands after each use children under 12 years: ask a doctor
- a dulifies and children 12 years and over

  use the tip of the cap to break the seal and open the tube

  use the tip of the cap to break the seal and open the tube

  wash the affected skin with soap and water and dry completely before applying

  a pply nonce a day to affected skin for 2 weeks or as directed by a doctor

  user hands after askin to a search and a search are a search and a search are a search and a search are a search and a search and a search and a search and a search a search and a

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away. Stop use and ask a doctor if too much irritation occurs or gets worse

When using this product do not get into the eyes. If eye contact occurs, rinse eyes thoroughly with water Do not use ■ on nails or scalp ■ in or near the mouth or the eyes ■ for vaginal yeast infections

For external use only Warnings

- relieves itching, burning, cracking, and scaling which accompany this condition
  - cures most jock itch รอรก

**Purpose** Antifungal **Active ingredient** Butenafine hydrochloride 1%

Drug Facts

LOTISIAN WILL BUTCHOTHE Cream 1%

BAR CODE

OTRIMINultra

- · Relieves Itching and Burning
- Full Prescription Strength





butenafine hydrochloride cream 1% **ANTIFUNGAL** 

Net Wt 24g (0.85 oz)

moo.nimirtol.www ts zu tisiv

**ANTIFUNGAL** butenafine hydrochloride cream 1%



7 week twice a day or

186u **026** 

Visit us at **www.lotrimin.com** © 2007 Distributed by Schering-Plough HealthCare Products, Inc., Memphis, TN 38151 J.A.2.U Mi rights reserved. Made in J.S.A. 23775-00

**Inactive ingredients** benzyl alcohol, cetyl alcohol, diethanolamine, glycerin, glyceryl monostearate SE, polyoxyethylene (23) cetyl ether, propylene glycol dicapnylate, purified water, sodium benzoate, stearic acid, white petrolatum

Other information 

do not use if seal on tube is broken or is not visible 
store at 5° - 30°C (41° - 86°F)

- children under 12 years: ask a doctor
- Lies the tip of the cap to break the seal and open the tube
   wash the affected skin with scap and water and dry completely before applying
   for affilet's a foot between the foes; apply to affected skin between and around the toes twice
   for affilet's a foot between the foes; apply to affected skin to the set affected by a doctor.
   West well-litting, ventilated shoes. Change shoes and socks at least once daily.
   for jock itch and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor.
   for jock itch and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor.
   for jock lich and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor.

PLOP USE AND ASK A GOCIOF IT 100 MUCH IFFICH OCCUFS OF GEIS WOFSE

- burning, cracking, and scaling which accompany these conditions
- nost athlete's foot between the toes. Effectiveness on the bottom or sides of foot is unknown.

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butensfine hydrochloride cream 1%

LOTRIMIN<mark>ülträ</mark>



Food and Drug Administration Rockville MD 20857

### **Division of Dermatologic and Dental Drug Products**

Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard, HFD-540
Rockville, MD 20850

### **FACSIMILE TRANSMISSION**

DATE: December 7, 2001 Number of Pages (including cover sheet) – 18

TO: Mary E. Williams, Associate Director, Regulatory Affairs

COMPANY: Schering-Plough HealthCare Products

FAX #: 908-679-1741

MESSAGE: Attached to this facsimile transmission, please find a copy of our Action Letter for your

NDA 21-307, Lotrimin Ultra butenafine HCl cream, 1%.

Thank you.

FROM: Frank H. Cross, Jr., M.A., CDR, Senior Regulatory Management Officer

PHONE #: 301-827-2063

FAX #: 301-827-2075/2091

and

FROM: Daniel P. Keravich, R.Ph., M.B.A., Regulatory Project Manager

PHONE #: 301-827-2248 FAX #: 301-827-2316

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Food and Drug Administration Rockville MD 20857

NDA 21-307

Schering-Plough HealthCare Products Attention: Mary E. Williams, Associate Director, Regulatory Affairs Three Connell Drive P.O. Box 603 Berkeley Heights, New Jersey 07922-0603

Dear Ms. Williams:

Please refer to your new drug application (NDA) dated September 28, 2000, received September 29, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for butenafine hydrochloride cream, 1%.

Please also refer to our Approvable Letter for Lotrimin Ultra butenafine hydrochloride cream 1% dated July 27, 2001.

We acknowledge receipt of your submissions dated October 5, November 5, and December 3 and 7 (facsimile), 2001.

This new drug application provides for the use without prescription of Lotrimin Ultra butenafine hydrochloride cream 1%, for the topical treatment of the following superficial dermatophytoses: interdigital tinea pedis (athlete's foot), tinea corporis (ringworm) and tinea cruris (jock itch) due to *E. floccosum*, *T. mentagrophytes*, *T. rubrum*, and *T. tonsurans*.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, immediate container and carton labels) and must be formatted in accordance with the requirements of 21 CFR 201.66. Marketing the product with FPL that is not identical to the approved labeling text and "Drug Facts" format may render the product misbranded and an unapproved new drug.

We note that copies of final printed labeling (FPL) have been submitted on October 5, 2001.

We remind you of your postmarketing study commitments in your submissions dated July 25, December 3 and 7 (facsimile), 2001. These commitments are listed below.

1. Conduct a study to test consumers= ability to differentiate the Lotrimin AF labeling from the Lotrimin Ultra labeling in terms of distinguishing the different active ingredients

Protocol Submission: Within 1 month of the date of this letter submit the

protocol for Agency review and approval.

Study Start: Within 3 months of the date of this letter initiate the study.

Final Report Submission: Within 6 months of the date of this letter submit the final

report.

2. Conduct a study to evaluate the safety of this drug for tinea corporis in the 2 - 12 year old pediatric population. This study should include pharmacokinetic sampling (systemic absorption data under maximal use conditions) and a comprehensive evaluation of local intolerance. Any additional information regarding local effects in children may be submitted, if available.

Protocol Submission: Within 3 months of the date of this letter submit the

protocol for Agency review and approval and any additional information regarding local effects in

children.

Study Start: Within 6 months of the date of this letter initiate the study.

Final Report Submission: Within 16 months of the date of this letter submit the final

report.

3. Conduct a study to evaluate the efficacy of this drug for tinea corporis in the 2 - 12 year old pediatric population, especially since the dermatophyte species responsible may vary from adults. Alternatively, information may be submitted that demonstrates that the dermatophyte species responsible for tinea corporis in the 2 - 12 year old pediatric population does not vary from adults. If this information is demonstrated, the need for an efficacy study could be waived.

Protocol Submission: Within 3 months of the date of this letter submit the

protocol and alternative information for Agency review

and approval.

Study Start: Within 9 months of the date of this letter initiate the study,

if the FDA concludes that the alternative information is not

convincing.

Final Report Submission: Within 19 months of the date of this letter submit the final

report.

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study.

All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled 'Postmarketing Study Protocol'', ''Postmarketing Study Final Report'', or ''Postmarketing Study Correspondence.''

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 FR 66632). Because of the low prevalence of tinea cruris and tinea pedis in the 12 year old and under pediatric population these indications would be difficult to study and are waived. Additionally, because of the low prevalence of tinea corporis in the 2 year old and under pediatric population this indication would be difficult to study and is waived. We note that you have not fulfilled the requirements of 21 CFR 314.55 (or 601.27) for pediatric studies in pediatric patients aged 2-12 years old for tinea corporis. We are deferring submission of these pediatric studies until April 7, 2003, for the pediatric safety study and July 7, 2003, for the pediatric efficacy study. We note your submission of a protocol to study tinea corporis in the 2-12 year old pediatric population.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at <a href="https://www.fda.gov/cder/pediatric">www.fda.gov/cder/pediatric</a>) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

In addition, please submit two copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Dermatologic & Dental Drug Products, one to the Division of Over-the-Counter Drug Products. For administrative purposes, this submission should be sent to the NDA and should be identified as a correspondence to approved NDA 21-307.

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements set forth under 21 CFR 314.80 and 314.81 for an approved NDA.

In line with Center for Drug Evaluation and Research policy, oversight of this application is being transferred to the Division of Over-the-Counter Drug Products. If you have any questions, please contact Daniel Keravich, Regulatory Health Project Manager, at (301) 827-2222.

### Sincerely,

{See appended electronic signature page}

Charles Ganley, M.D.

Director

Division of Over-The-Counter Drug Products

Office of Drug Evaluation V

Center for Drug Evaluation and Research

{See appended electronic signature page}

Jonathan K. Wilkin, M.D.

Director

Division of Dermatologic & Dental Drug Products

Office of Drug Evaluation V

Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

\_\_\_\_\_\_

Charles Ganley 12/7/01 03:53:09 PM

Jonathan Wilkin 12/7/01 04:04:16 PM



23562-00

Net Wt 12g (0.42 oz)

Active ingredient
Butenafine hydrochloride 1%...

**Purpose** .....Antifungal

**Uses** • cures most athlete's foot between the toes, jock itch and ringworm • relieves itching, burning, cracking, and scaling which accompany these conditions

releves nching, ourning, cracking, also scanny minor sections by Warnings
 To external use only
 To not use • on nails or scalp • in or near the mouth or the eyes • for vaginal yeast infections
 When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water.
 Stop use and ask a doctor if too much irritation occurs or gets worse.
 Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.
 Aircections

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.

Directions

- adults and children 12 years and older

- use the tip of the cap to break the seal and open the tube

- use the tip of the cap to break the seal and open the tube

- use the tip of the cap and water and dry completely before applying

- for athlete's foot between the foes: apply to affected skin between and around the toes twice a day for 1 weeks, or as directed by a doctor.

Wear well-fitting, ventilated shoes. Change shoes and socks at least once daily.

- for jock ith and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor

- wash hands after each use

- children under 12 years: ask a doctor

Store at 5° - 30°C (41° - 86°F). See crimp for lot number and expiration date

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23564-00

Net Wt 24g (0.85 oz)

Active ingredient
Butenafine hydrochloride 1%...

**Purpose** ..Antifungal

Uses
■ Cures most athlete's foot between the toes, jock itch and ringworm
■ relieves itching, burning, cracking, and scaling which accompany these conditions Warnings For external use only

Do not use

on nails or scalp

in or near the mouth or the eyes

for vaginal yeast infections

When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water.

Stop use and ask a doctor if too much irritation occurs or gets worse.

**Keep out of reach of children.** If swallowed, get medical help or contact a Poison Control Center right away.

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.

Directions

- adults and children 12 years and older

- use the tip of the cap to break the seal and open the tube

- wash the affected skin with soap and water and dry completely before applying

- for athlete's foot between the foes: apply to affected skin between and around the toes twice a day for 1 week (morning and night), or once a day for 4 weeks, or as directed by a doctor. Wear well-fitting, ventilated shoes. Change shoes and socks at least once daily.

- for jock itch and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor

- wash hands after each use

- children under 12 years: ask a doctor

Store at 5° - 30°C (41° - 86°F). See crimp for lot number and expiration date ©2001 Distributed by Schering-Plough HealthCare Products, Inc., Memphis, TN 38151 U.S.A. All rights reserved. Made in U.S.A.



ANTIFUNGAL

Active ingredient
Butenafine hydrochloride 1%.

**Purpose** ...Antifungal

Net Wt 12g (0.42 oz)

23565-00

Uses

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right:

Directions

- adults and children 12 years and older

- use the tip of the cap to break the seal and open the tube

- wash the affected skin with spap and water and dry completely before applying

- apply once a day to affected skin for 2 weeks or as directed by a doctor

- wash hands after each use

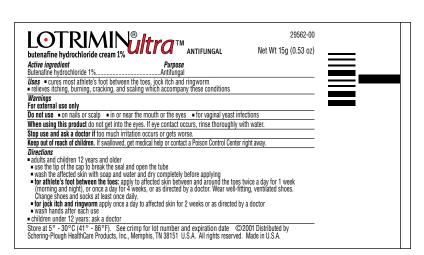
- children under 12 years: ask a doctor

Store at \$5^- > 0.0^- (At 1° - 86°F). See crimp for lot number and expiration date

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- · Relieves Itching and Burning
- \*Full Prescription Strength





Net Wt 15g (0.53 oz)



1 week twice a day or 4 weeks once a day

**920q1u¶** IsgnutitnA .

2901 941 Apply between and aroung







Wist us at www.lotrimin.com © Constributed by Schering-Plough HealthCare Products, Inc., Memphis, TV 188.U 16.A. A.D. Inghts reserved. Made in J.S.U in Made i 59229-00

**Inactive ingredients** benzyl alcohol, cetyl alcohol, diethanolamine, glycerin, glyceryl monostearate SE, polyoxyethylene (23) cetyl ether, propylene glycol dicapnylate, purfiled water, sodium benzoate, stearic acid, white petrolatum

■ do not use if seal on tube is broken or is not visible ■ store at 5° - 30°C (41° - 86°F)

Other information

- children under 12 years: ask a doctor
- uses the tip of the cap to bresk the seal and open the tube
   uses the tip of the cap to bresk the seal and once a day for 4 weeks, or as directed by a doctor. Wear well-fitting, vernitisted shoes. Change shoes and socks at least once daily.
   for 1 week (morning and night), or once a day for 4 weeks, or as directed by a doctor. Wear well-fitting, vernitisted shoes. Change shoes and socks at least once daily.
   for 1 week (morning and night), or once a day for 4 weeks, or as directed by a doctor.
  - - - - adults and children 12 years and older

**Keep out of reach of children.** If swallowed, get medical help or contact a Poison Control Center right away Stop use and ask a doctor if too much irritation occurs or gets worse

When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water. ■ in or near the mouth or the eyes

- relieves itching, burning, cracking, and scaling which accompany these conditions
- cures most athlete's foot between the foes. Effectiveness on the bottom or sides of foot is unknown.

   cures most jock itch and ingworm

Active ingredient
% t əbirolhorbyd ənitənətu

Drug Facts

Dutenafine hydrochloride cream 1% ULT STATE





- · Relieves Itching, **Burning** and Chafing
- Full Prescription Strength



# butenafine hydrochloride cream 1%



Net Wt 15g (0.53 oz)





wisit us at www.lotrimin.com

butenafine hydrochloride cream 1%

Wist us at www. Jotinmin.com © 2001 Distributed by Schering-Plough HealthCare Products, Inc., Memphis, TN 38151 U.S.A. All rights reserved. Made in U.S.A.

**Inactive ingredients** benzyl alcohol, celyl alcohol, diethanolamine, glycerin, glyceryl monostearate SE, polyoxyethylene (23) celyl ether, propylene glycol dicapnylate, purflied water, sodium benzoate, stearic acid, white petrolatum

- Other information

  do not use if seal on tube is broken or is not visible

  store at 5° 30°C (41° 86°F)
  - - children under 12 years: ask a doctor
- adults and children 12 years and over

  use the tip of the cap to break the seal and open the tube

  wash the affected skin with soap and water and dry completely before applying

  a wash tone a day to affected skin for 2 weeks or as directed by a doctor

  a apply once a day to affected skin for 2 weeks or as directed by a doctor

  a part of the complete standard or a search or a

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away

Stop use and ask a doctor if too much irritation occurs or gets worse

When using this product do not get into the eyes. If eye contact occurs, rinse eyes thoroughly with water Do not use  $\blacksquare$  on nails or scalp  $\blacksquare$  in or near the mouth or the eyes  $\blacksquare$  for vaginal yeast infections

For external use only **SgninnsW** 

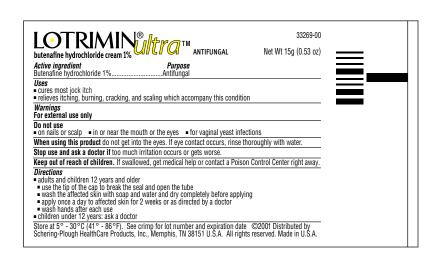
- relieves itching, burning, cracking, and scaling which accompany this condition
  - cures most jock itch

**Purpose** Antifungal **Active ingredient** Butenafine hydrochloride 1%

Drug Facts

LOTRIMIL<sup>®</sup>UÉRA





- Relieves Itching and Burning
- Full Prescription Strength



butenafine hydrochloride cream 1% **ANTIFUNGAL** 

Net Wt 30g (1.1 oz)



1 week twice a day or 4 weeks once a day

Apply between and around the toes



wisit us at www.lotrimin.com

**JADNUJITNA** butenafine hydrochloride cream 1%

00-19967 © 2001 Distributed by Schering-Plough HealthOare Products, Inc., Memphis, TN 38151 U.S.A. All rights reserved. Made in U.S.A.

**Inactive ingredients** benzyl alcohol, cetyl alcohol, diethanolamine, glycerin, glyceryl monostearate SE, polyoxyethylene (23) cetyl ether, propylene glycol dicaprylate, purfled water, sodium benzoate, stearic acid, white petrolatum

Other information = do not use if seal on tube is broken or is not visible (\* 7° - 8° 7°)

- eachurs and cnilioren 12 years and older
   wash the set be best the seal and open the tube
   wash the affected skin with soap and water and dry completely before applying
   wash the affected skin with soap and water and dry completely before applying
   for althete's foot between the loses; apply to affected skin between and around the toes fwice a day
   for lock litch and ringworm apply once a day for 4 weeks, or as directed by a doctor. Wear well iffing, venifiated shoes. Change shoes and socks at lesst once daily.

   iffing, venifiated shoes. Change shoes and socks at lesst once a daily.

   if or Jock litch and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor.

   in a day to a day to affect a skin for 2 weeks or as directed by a doctor.

   in a day to a day to affect a skin for 2 weeks or as directed by a doctor.

   in a day to a day to affect a skin for 2 weeks or as directed by a doctor.

   in a day to a day to

op use and ask a doctor if too much irritation occurs or gets worse

When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water. Do not use ■ on nails or scalp ■ in or near the mouth or the eyes ■ for vaginal yeast infections

- telleves tiching, burning, cracking, and scaling which accompany these conditions
- nost athlete's foot between the toes. Effectiveness on the bottom or sides of foot is unknown.

esoqnu¶	ting ingredient
	nd Facts

MINITERIAL STREET TO THE PROPERTY OF THE PROPE

OTRIMINultra



LOTRIMIN<sup>®</sup> ANTIFUNGAL butenafine hydrochloride cream 1% **Purpose** .Antifungal Active ingredient
Butenafine hydrochloride 1%

29560-00

Net Wt 30g (1.1 oz)

Uses

Uses

cures most athlete's foot between the toes, jock itch and ringworm
relieves itching, burning, cracking, and scaling which accompany these conditions

Warnings
For external use only

Do not use
on nalis or scalp
in or near the mouth or the eyes
for vaginal yeast infections

When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water.

Stop use and ask a doctor if too much irritation occurs or gets worse.

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.

Directions

Keep out of reach of children. It Swallowed, your model.

Directions

adults and children 12 years and older

use the tip of the cap to break the seal and open the tube

wash the affected skin with soap and water and dry completely before applying

for athlete's foot between the toes: apply to affected skin between and around the toes twice a day for 1 week (morning and night), or once a day for 4 weeks, or as directed by a doctor. Wear well-fitting, ventilated shoes. Change shoes and socks at least once daily.

for jock itch and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor

wash hands after each use

children under 12 years: ask a doctor

Store at 5° - 30° C (41° - 86°F). See crimp for lot number and expiration date @2001 Distributed by Schering-Plough HealthCare Products, Inc., Memphis, TN 38151 U.S.A. All rights reserved. Made in U.S.A.





# butenafine hydrochloride cream 1%

**ANTIFUNGAL** 

## butenafine hydrochloride cream 1% ANTIFUNGAL

Net Wt 12g (0.42 oz)



1 week twice a day or 4 weeks once a day

bng netween and strong bround the foes



butenafine hydrochloride cream 1%

S.2073-00 @ A.2.U ni absM. Devrsean zitrigin IIA. A.2.U 12186 NT , ainfimmM, and its reserved. Made in Made in M.2.U ni absM. Devrsean inghts reserved.

**Inactive ingredients** benzyl alcohol, cetyl alcohol, diethanolamine, glycerin, glyceryl monostearate SE, polyoxyethylene (23) cetyl ether, propylene glycol dicaprylate, purified water, sodium benzoate, stearic acid, white petrolatum

■ do not use if seal on tube is broken or is not visible ■ store at 5° - 30°C (41° - 86°F)

Other information

- children under 12 years: ask a doctor
- for lock itch and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor wash hands affer each use
- adults and children 12 years and older adultion 12 years and older and the table and the cap to break the seal and open the tube

   wash the disclered stim with soap and waiter and dry completely before applying
   for shicle's foot between the foes: apply to affected skin between and around the toes twice a day for 1 week (morning and night), or once a day for 4 weeks, or as diest once a day for 4 weeks, or as diest once a day for 1 week once and accorded by a doctor. Wear well-filling, ventilated shoes. Change shoes and accoks a least once daily.

ceep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away. Stop use and ask a doctor if too much irritation occurs or gets worse

When using this product do not get into the eyes. If eye contact occurs, rinse thoroughly with water. Do not use ■ on nails or scalp ■ in or near the mouth or the eyes ■ for vaginal yeast infections

For external use only

- Warnings
- cures most athlete's foot between the toes. Effectiveness on the bottom or sides of foot is unknown.
   cures most jock itch and ringworm
   relieves itching, burning, cracking, and scaling which accompany these conditions

Purpose Antifungal

**Active ingredient** Wr ebirochloorbyn enitsnetu

Drug Facts

LOTISIANI SUITE Dutensfine hydrochloride cream 1%

LOTRIMIN*ultra*"



OTRIMIN<sup>®</sup> butenafine hydrochloride cream 1% **ANTIFUNGAL** 

## butenafine hydrochloride cream 1% **ANTIFUNGAL**

Net Wt 12g (0.42 oz)

BAR CODE



moo.nimirtol.www ts zu tisiv carton carton

butenafine hydrochloride cream 1%

23778-00

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**Inactive ingredients** benzyl alcohol, cetyl alcohol, diethanolamine, glycerin, glyceryl monostearate SE, polyoxyethylene (23) cetyl ether, propylene glycol dicapnylate, purfled water, sodium benzoate, stearic acid, white petrolatum

- **Other information**do not use if seal on tube is broken or is not visible

  do not use if \$6 30°C (41° 86°F)

  - wash hands after each use children under 12 years: ask a doctor
- a dulifies and children 12 years and over

  use the tip of the cap to break the seal and open the tube

  use the tip of the cap to break the seal and open the tube

  wash the affected skin with soap and water and dry completely before applying

  a pply nonce a day to affected skin for 2 weeks or as directed by a doctor

  user hands after askin to a search and a search are a search and a search are a search and a search are a search and a search and a search and a search and a search a search and a

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away. Stop use and ask a doctor if too much irritation occurs or gets worse When using this product do not get into the eyes. If eye contact occurs, rinse eyes thoroughly with water

Do not use ■ on nails or scalp ■ in or near the mouth or the eyes ■ for vaginal yeast infections

For external use only Warnings

- relieves itching, burning, cracking, and scaling which accompany this condition
  - cures most jock itch

รอรก

**Purpose** Antifungal

**Active ingredient** Butenafine hydrochloride 1%

Drug Facts

LOTISIAN WILL BUTCHOTHE Cream 1%

BAR CODE

OTRIMINultra

- · Relieves Itching and Burning
- Full Prescription Strength





butenafine hydrochloride cream 1% **ANTIFUNGAL** 

Net Wt 24g (0.85 oz)

moo.nimirtol.www ts zu tisiv

**ANTIFUNGAL** butenafine hydrochloride cream 1%



7 week twice a day or

**Purpose** Antifungal

Visit us at **www.lotrimin.com** © 2007 Distributed by Schering-Plough HealthCare Products, Inc., Memphis, TN 38151 J.A.2.U Mi rights reserved. Made in J.S.A. 23775-00

**Inactive ingredients** benzyl alcohol, cetyl alcohol, diethanolamine, glycerin, glyceryl monostearate SE, polyoxyethylene (23) cetyl ether, propylene glycol dicapnylate, purified water, sodium benzoate, stearic acid, white petrolatum

### Other information do not use if seal on tube is broken or is not visible store at 5° - 30°C (41° - 86°F)

- children under 12 years: ask a doctor
- Lies the tip of the cap to break the seal and open the tube
   wash the affected skin with scap and water and dry completely before applying
   for affilet's a foot between the foes; apply to affected skin between and around the toes twice
   for affilet's a foot between the foes; apply to affected skin to the set affected by a doctor.
   West well-litting, ventilated shoes. Change shoes and socks at least once daily.
   for jock itch and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor.
   for jock itch and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor.
   for jock lich and ringworm apply once a day to affected skin for 2 weeks or as directed by a doctor.

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- ourning, cracking, and scaling which accompany these conditions

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butensfine hydrochloride cream 1%



MODE = MEMORY TRANSMISSION

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END=DEC-07 16:46

FILE NO. =413

STN COMM. NO.

ONE-TOUCH/ STATION NAME/EMAIL ADDRESS/TELEPHONE NO. ABBR NO.

**PAGES** 

DURATION

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-FDA/CDER/DDDDP/HFD54Ø

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### DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration Rockville MD 20857

### Division of Dermatologic and Dental Drug Products

Office of Drug Evaluation V Center for Drug Evaluation and Research Food and Drug Administration 9201 Corporate Boulevard, HFD-540 Rockville, MD 20850

### **FACSIMILE TRANSMISSION**

DATE:

December 7, 2001

Number of Pages (including cover sheet) -18

TO:

Mary E. Williams, Associate Director, Regulatory Affairs

COMPANY: Schering-Plough HealthCare Products

FAX #:

908-679-1741

MESSAGE:

Attached to this facsimile transmission, please find a copy of our Action Letter

for your NDA 21-307, Lotrimin Ultra butenafine HCl cream, 1%.

Thank you.

FROM:

Frank H. Cross, Jr., M.A., CDR, Senior Regulatory Management Officer

PHONE #: FAX #:

301-827-2063 301-827-2075/2091

and

FROM:

Daniel P. Keravich, R.Ph., M.B.A., Regulatory Project Manager

PHONE #: FAX#:

301-827-2248 301-827-2316

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