CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

65-085

Generic Name: Mupirocin Ointment USP, 2%

Sponsor: TEVA Pharmaceuticals USA

Approval Date: November 7, 2003

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-085

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-085

APPROVAL LETTER

ANDA 65-085

NOV 7 2003

TEVA Pharmaceuticals USA
Attention: Vincent Andolina
1090 Horsham Road
P.O. Box 1090
North Wales, PA 19454

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated January 11, 2001, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Mupirocin Ointment USP, 2%. We note that this product is subject to the exception provisions of Section 125(d)(2) of Title I of the Food and Drug Administration Modernization Act of 1997.

Reference is also made to your amendments dated January 21, April 9, May 3, August 23, and November 21, 2002; and June 17, and August 13, 2003.

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 labeling. Accordingly the application is approved. The Division of Bioequivalence has determined your Mupirocin Ointment USP, 2%, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Bactroban® Ointment, 2%, of GlaxoSmithKline).

Under Section 506A of the Act, 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.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print.

Submit both copies together with a copy of the final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FDA 2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

11/7/2003

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-085

FINAL PRINTED LABELING

1010

MUPIROCIN OINTMENT USP, 2%

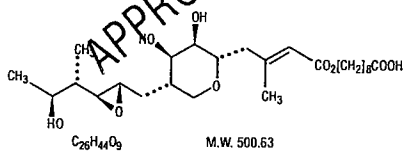
For Dermatologic Use

NOV - 7 2003

APPROVED

DESCRIPTION

Each gram of Mupirocin Ointment 2% contains 20 mg mupirocin in a bland water miscible ointment base (polyethylene glycol ointment, N.F.) consisting of polyethylene glycol 400 and polyethylene glycol 3350. Mupirocin is a naturally occurring antibiotic. The chemical name is (*E*)-(2*S*,3*R*,4*R*,5*S*)-5-[(2*S*,3*S*,4*S*,5*S*)-2,3-Epoxy-5-hydroxy-4-methylhexyl]tetrahydro-3,4-dihydroxy-6-methyl-2*H*-pyran-2-crotonic acid, ester with 9-hydroxynonanoic acid. The chemical structure is:



$C_{26}H_{44}O_9$ M.W. 500.63

CLINICAL PHARMACOLOGY

Application of ^{14}C-labeled mupirocin ointment to the lower arm of normal male subjects followed by occlusion for 24 hours showed no measurable systemic absorption (<1.1 nanogram mupirocin per milliliter of whole blood). Measurable radioactivity was present in the stratum corneum of these subjects 72 hours after application.

Following intravenous or oral administration, mupirocin is rapidly metabolized. The principal metabolite, monic acid, is eliminated by renal excretion, and demonstrates no antibacterial activity. In a study conducted in seven healthy adult male subjects, the elimination half-life after intravenous administration of mupirocin was 20 to 40 minutes for mupirocin and 30 to 80 minutes for monic acid. The pharmacokinetics of mupirocin has not been studied in individuals with renal insufficiency.

Microbiology: Mupirocin is an antibacterial agent produced by fermentation using the organism *Pseudomonas fluorescens*. It is active against a wide range of gram-positive bacteria including methicillin-resistant *Staphylococcus aureus* (MRSA). It is also active against certain gram-negative bacteria. Mupirocin inhibits bacterial protein synthesis by reversibly and specifically binding to bacterial isoleucyl transfer-RNA synthetase. Due to this unique mode of action, mupirocin demonstrates no *in vitro* cross-resistance with other classes of antimicrobial agents.

Resistance occurs rarely. However, when mupirocin resistance does occur, it appears to result from the production of a modified isoleucyl-tRNA synthetase. High-level plasmid-mediated resistance (MIC > 1024 mcg/mL) has been reported in some strains of *S. aureus* and coagulase-negative staphylococci.

Mupirocin is bactericidal at concentrations achieved by topical administration. However, the minimum bactericidal concentration (MBC) against relevant pathogens is generally eight-fold to thirty-fold higher than the minimum inhibitory concentration (MIC). In addition, mupirocin is highly protein bound (>97%), and the effect of wound secretions on the MICs of mupirocin has not been determined. Mupirocin has been shown to be active against most strains of *Staphylococcus aureus* and *Streptococcus pyogenes*, both *in vitro* and in clinical studies. (See **INDICATIONS AND USAGE**). The following *in vitro* data are available, BUT THEIR CLINICAL SIGNIFICANCE IS UNKNOWN. Mupirocin is active against most strains of *Staphylococcus epidermidis* and *Staphylococcus saprophyticus*.

INDICATIONS AND USAGE

Mupirocin ointment 2% is indicated for the topical treatment of impetigo due to: *Staphylococcus aureus* and *Streptococcus pyogenes*.

CONTRAINDICATIONS

This drug is contraindicated in individuals with a history of sensitivity reactions to any of its components.

WARNINGS

Mupirocin ointment is not for ophthalmic use.

PRECAUTIONS

If a reaction suggesting sensitivity or chemical irritation should occur with use of mupirocin ointment 2%, treatment should be discontinued and appropriate alternative therapy for the infection instituted.

As with other antibacterial products prolonged use may result in overgrowth of nonsusceptible organisms, including fungi.

Mupirocin ointment is not formulated for use on mucosal surfaces. Intranasal use has been associated with isolated reports of stinging and drying. A paraffin-based formulation – *Bactroban® Nasal (mupirocin calcium ointment) – is available for intranasal use.

Polyethylene glycol can be absorbed from open wounds and damaged skin and is excreted by the kidneys. In common with other polyethylene glycol-based ointments, mupirocin ointment should not be used in conditions where absorption of large quantities of polyethylene glycol is possible, especially if there is evidence of moderate or severe renal impairment.

Information for Patients: Use this medication only as directed by your health provider. It is for external use only. Avoid contact with the eyes. The medication should be stopped and your health care practitioner contacted if irritation, severe itching, or rash occurs.

If impetigo has not improved in 3 to 5 days, contact your health care practitioner.

Drug Interactions: The effect of the concurrent application of mupirocin ointment and other drug products has not been studied.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals to evaluate carcinogenic potential of mupirocin have not been conducted.

Results of the following studies performed with mupirocin calcium or mupirocin sodium *in vitro* and *in vivo* did not indicate a potential for genotoxicity: rat primary hepatocyte unscheduled DNA synthesis, sediment analysis for DNA strand breaks, *Salmonella* reversion test (Ames), *Escherichia coli* mutation assay, metaphase analysis of human lymphocytes, mouse lymphoma assay, and bone marrow micronuclei assay in mice.

Reproduction studies were performed in male and female rats with mupirocin administered subcutaneously at doses up to 14 times a human topical dose (approximately 60 mg mupirocin per day) on a mg/m^2 basis and revealed no evidence of impaired fertility and reproductive performance from mupirocin.

Pregnancy: Teratogenic Effects: Pregnancy Category B: Reproduction studies have been performed in rats and rabbits with mupirocin administered subcutaneously at doses up to 22 and 43 times, respectively, the human topical dose (approximately 60 mg mupirocin per day) on a mg/m^2 basis and revealed no evidence of harm to the fetus due to mupirocin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when mupirocin ointment is administered to a nursing woman.

Pediatric Use: The safety and effectiveness of mupirocin ointment have been established in the age range of 2 months to 16 years. Use of mupirocin ointment in these age groups is supported by evidence from adequate and well-controlled studies of mupirocin ointment in impetigo in pediatric patients studied as a part of the pivotal clinical trials (See **CLINICAL STUDIES**).

ADVERSE REACTIONS

The following local adverse reactions have been reported in connection with the use of mupirocin ointment: burning, stinging, or pain in 1.5% of patients; itching in 1% of patients; rash, nausea, erythema, dry skin, tenderness, swelling, contact dermatitis, and increased exudate in less than 1% of patients.

DOSAGE AND ADMINISTRATION

A small amount of mupirocin ointment should be applied to the affected area three times daily. The area treated may be covered with a gauze dressing if desired. Patients not showing a clinical response within 3 to 5 days should be reevaluated.

CLINICAL STUDIES

The efficacy of topical mupirocin ointment in impetigo was tested in two studies. In the first, patients with impetigo were randomized to receive either mupirocin ointment or vehicle placebo t.i.d. for 8 to 12 days. Clinical efficacy rates at end of therapy in the evaluable populations (adults and pediatric patients included) were 71% for mupirocin ointment (n=49) and 35% for vehicle placebo (n=51). Pathogen eradication rates in the evaluable populations were 94% for mupirocin ointment and 62% for vehicle placebo. There were no side effects reported in the group receiving mupirocin ointment.

In the second study, patients with impetigo were randomized to receive either mupirocin ointment t.i.d. or 30 to 40 mg/kg oral erythromycin ethylsuccinate per day (this was an unblinded study) for 8 days. There was a follow-up visit 1 week after treatment ended. Clinical efficacy rates at the follow-up visit in the evaluable populations (adults and pediatric patients included) were 93% for mupirocin ointment (n=29) and 78.5% for erythromycin (n=28). Pathogen eradication rates in the evaluable patient populations were 100% for both test groups. There were no side effects reported in the mupirocin ointment group.

Pediatrics: There were 91 pediatric patients aged 2 months to 15 years in the first study described above. Clinical efficacy rates at end of therapy in the evaluable populations were 78% for mupirocin ointment (n=42) and 36% for vehicle placebo (n=49). In the second study described above, all patients were pediatric except two adults in the group receiving mupirocin ointment. The age range of the pediatric patients was 7 months to 13 years. The clinical efficacy rate for mupirocin ointment (n=27) was 96%, and for the erythromycin it was unchanged (78.5%).

HOW SUPPLIED

Mupirocin Ointment USP, 2% is supplied in 15 gram, 22 gram, and 30 gram tubes.

Store at controlled room temperature 15° to 30°C (59° to 86°F) (see USP).

*Bactroban® Nasal is a registered trademark of SmithKline Beecham Pharmaceuticals.

Manufactured By:
TEVA PHARMACEUTICALS USA
Sellersville, PA 18960

Rev. D 4/2003

65-085
APP
11-7-03

NDC 0093-1010-15

MUPIROCIN OINTMENT, USP
2%

15 GRAMS
TEVA

For Dermatologic Use Only. Not For Ophthalmic Use.

APPROVED
NOV - 7 2003
126

Usual Dosage: For dermatologic use only. Apply a small amount of ointment to the affected area three times daily. Patients not showing a clinical response within 3 to 5 days should be reevaluated. See accompanying prescribing information.

℞ only

Store at controlled room temperature 15° to 30°C (59° to 86°F)(see USP).

For control number and expiration date, see crimp.

Each gram contains 20 mg mupirocin in a polyethylene glycol ointment, NF base.

KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

C20733

TEVA PHARMACEUTICALS USA, Sellersville, PA 18960

Iss. 5/2001

NDC 0093-1010-42

MUPIROCIN OINTMENT, USP
2%

22 GRAMS
TEVA

For Dermatologic Use Only. Not For Ophthalmic Use.

NOV - 7 2003

APPROVED
115

Usual Dosage: For dermatologic use only. Apply a small amount of ointment to the affected area three times daily. Patients not showing a clinical response within 3 to 5 days should be reevaluated. See accompanying prescribing information.

℞ only

Store at controlled room temperature 15° to 30°C (59° to 86°F) (see USP).

For control number and expiration date, see crimp.

Each gram contains 20 mg mupirocin in a polyethylene glycol ointment, NF base.

KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

TEVA PHARMACEUTICALS USA, Sellersville, PA 18960

C20736

Iss. 4/2002

NDC 0093-1010-30

MUPIROCIN OINTMENT, USP
2%

30 GRAMS
TEVA

For Dermatologic Use Only. Not For Ophthalmic Use.

APPROVED
125
NOV - 7 2003

Usual Dosage: For dermatologic use only. Apply a small amount of ointment to the affected area three times daily. Patients not showing a clinical response within 3 to 5 days should be reevaluated. See accompanying prescribing information.

℞ only

Store at controlled room temperature 15° to 30°C (59° to 86°F)(see USP).

For control number and expiration date, see crimp.

Each gram contains 20 mg mupirocin in a polyethylene glycol ointment, NF base.

KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

C20731

TEVA PHARMACEUTICALS USA, Sellersville, PA 18960

Iss. 5/2001

65-085
APP 11-7-03

NDC 0093-1010-15

MUPIROCIN OINTMENT, USP 2%

℞ only

15 GRAMS

TEVA

For Dermatologic Use Only. Not For Ophthalmic Use.

Usual Dosage: For dermatologic use only. Apply a small amount of ointment to the affected area three times daily. Patients not showing a clinical response within 3 to 5 days should be reevaluated. See accompanying prescribing information.

Information for Patients: Use this medication only as directed by your health provider. It is for external use only. Avoid contact with the eyes. The medication should be stopped and your health care practitioner contacted if irritation, severe itching, or rash occurs.

If impetigo has not improved in 3 to 5 days, contact your health care practitioner.

Mat. No. C20732

MUPIROCIN OINTMENT, USP 2% 15 GRAMS

PG Iss. 8/2002

NDC 0093-1010-15

MUPIROCIN OINTMENT, USP 2%

℞ only

15 GRAMS

TEVA

For Dermatologic Use Only. Not For Ophthalmic Use.

APPROVED NOV - 7 2003

Each gram contains: 20 mg mupirocin in a polyethylene glycol ointment, NF base.

For control number and expiration date, see crimp.

Store at controlled room temperature 15° to 30°C (59° to 86°F)(see USP).

KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

TEVA PHARMACEUTICALS USA, Sellersville, PA 18960

N 3 0093-1010-15 5 00

Mat. No. C20732

NDC 0093-1010-42

MUPIROCIN OINTMENT, USP

2%

℞ only

22 GRAMS

TEVA

For Dermatologic Use Only. Not For Ophthalmic Use.

NOV - 7 2003

APPROVED

Usual Dosage: For dermatologic use only. Apply a small amount of ointment to the affected area three times daily. Patients not showing a clinical response within 3 to 5 days should be reevaluated. See accompanying prescribing information.

Information for Patients: Use this medication only as directed by your health provider. It is for external use only. Avoid contact with the eyes. The medication should be stopped and your health care practitioner contacted if irritation, severe itching, or rash occurs.

If impetigo has not improved in 3 to 5 days, contact your health care practitioner.

Mat. No. C20734

MUPIROCIN OINTMENT, USP 2% 22 GRAMS

NDC 0093-1010-42

MUPIROCIN OINTMENT, USP

2%

℞ only

22 GRAMS

TEVA

For Dermatologic Use Only. Not For Ophthalmic Use.

Each gram contains: 20 mg mupirocin in a polyethylene glycol ointment, NF base.

For control number and expiration date, see crimp.

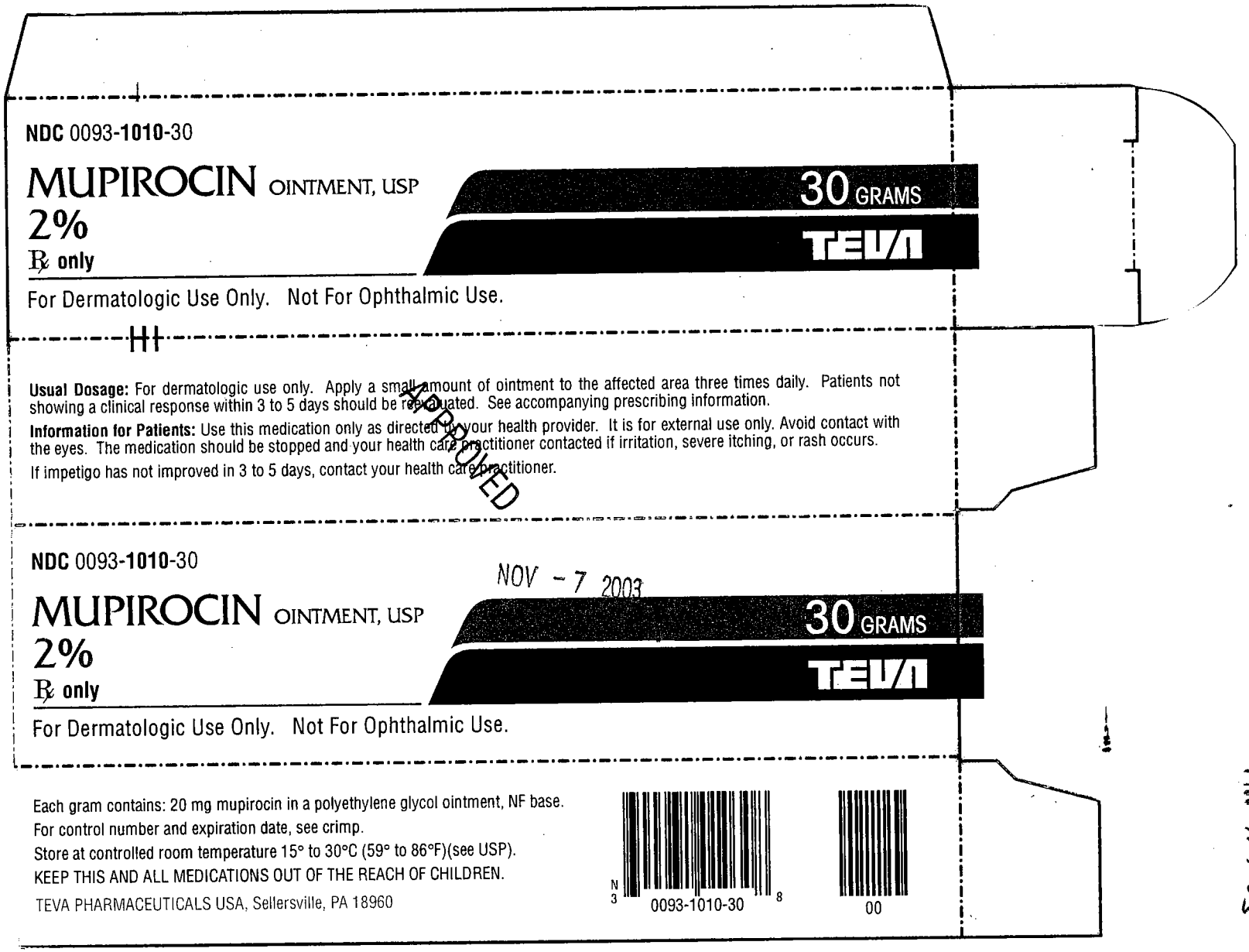
Store at controlled room temperature 15° to 30°C (59° to 86°F)(see USP).

KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

TEVA PHARMACEUTICALS USA, Sellersville, PA 18960

N 3 0093-1010-42 1 00

Mat. No. C20734



65-085
AP 11-7-03

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-085

CSO LABELING REVIEW(S)

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

ANDA Number: **65-085** Date of Submission: **January 11, 2001**

Applicant's Name: **TEVA Pharmaceuticals USA**

Established Name: **Mupirocin Ointment USP, 2%**

Labeling Deficiencies:

1. GENERAL COMMENT:

   Revise the storage temperature recommendation throughout your labels and labeling as follows:

   Store at controlled room temperature 15° to 30°C (59° to 86°F)(see USP).

2. CONTAINER 15 gram and 30 gram

   a. See GENERAL COMMENT above.

   b. "For dermatologic use only."

   c. Add the statement "Not for ophthalmic use."

   d. Side Panel – "reevaluated" (delete the ~~~~

3. CARTON 1 x 15 gram and 1 x 30 gram

   See comments under CONTAINER.

4. INSERT

   a. DESCRIPTION

      Add the molecular weight (500.63) and the molecular formula ($C_{26}H_{44}O_9$) to this section.

   b. CLINICAL PHARMACOLOGY

      i. Delete the first paragraph (the current second paragraph becomes the first paragraph).

      ii. Add the following text as the second paragraph:

      Following intravenous or oral administration, mupirocin is rapidly metabolized. The principal metabolite, monic acid, is eliminated by renal excretion, and demonstrates no antibacterial activity. In a study conducted in seven healthy adult male subjects, the elimination half-life after intravenous administration of mupirocin was 20 to 40 minutes for mupirocin and 30 to 80 minutes for monic acid. The pharmacokinetics of mupirocin has not been studied in individuals with renal insufficiency.

iii. Microbiology – Revise this subsection as follows:

Microbiology: Mupirocin is an antibacterial agent produced by fermentation using the organism *Pseudomonas fluorescens*. It is active against a wide range of gram-positive bacteria including methicillin-resistant *Staphylococcus aureus* (MRSA). It is also active against certain gram-negative bacteria. Mupirocin inhibits bacterial protein synthesis by reversibly and specifically binding to bacterial isoleucyl transfer-RNA synthetase. Due to this unique mode of action, mupirocin demonstrates no *in vitro* cross-resistance with other classes of antimicrobial agents.

Resistance occurs rarely. However, when mupirocin resistance does occur, it appears to result from the production of a modified isoleucyl-tRNA synthetase. High-level plasmid-mediated resistance (MIC > 1024 mcg/mL) has been reported in some strains of *S. aureus* and coagulase-negative staphylococci.

Mupirocin is bactericidal at concentrations achieved by topical administration. However, the minimum bactericidal concentration (MBC) against relevant pathogens is generally eight-fold to thirty-fold higher than the minimum inhibitory concentration (MIC). In addition, mupirocin is highly protein bound (>97%), and the effect of wound secretions on the MICs of mupirocin has not been determined. Mupirocin has been shown to be active against most strains of *Staphylococcus aureus* and *Streptococcus pyogenes*, both *in vitro* and in clinical studies. (See **INDICATIONS AND USAGE**). The following *in vitro* data are available, BUT THEIR CLINICAL SIGNIFICANCE IS UNKNOWN. Mupirocin is active against against most strains of *Staphylococcus epidermidis* and *Staphylococcus saprophyticus*.

c. INDICATIONS AND USAGE

i. "... *aureus* and *Streptococcus pyogenes*."

ii. Delete the asterisked statements.

d. CONTRAINDICATIONS

"... contraindicated in individuals ..." (add "in")

e. PRECAUTIONS

i. Third paragraph – "... and drying. A paraffin-based formulation – Bactroban® Nasal (mupirocin calcium ointment) – is available for intranasal use.

ii. Add the following subsections after the fourth paragraph:

Information for Patients: Use this medication only as directed by your healthcare provider. It is for external use only. Avoid contact with the eyes. The medication should be stopped and your healthcare practitioner contacted if irritation, severe itching, or rash occurs.

If impetigo has not improved in 3 to 5 days, contact your healthcare practitioner.

Drug Interactions: The effect of the concurrent application of mupirocin ointment and other drug products has not been studied.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals to evaluate carcinogenic potential of mupirocin have not been conducted.

Results of the following studies performed with mupirocin calcium or mupirocin sodium *in vitro* and *in vivo* did not indicate a potential for genotoxicity: rat primary hepatocyte unscheduled DNA synthesis, sediment analysis for DNA strand breaks, *Salmonella* reversion test (Ames), *Escherichia coli* mutation assay, metaphase analysis of human lymphocytes, mouse lymphoma assay, and bone marrow micronuclei assay in mice.

Reproduction studies were performed in male and female rats with mupirocin administered subcutaneously at doses up to 14 times a human topical dose (approximately 60 mg mupirocin per day) on a mg/m^2 basis and revealed no evidence of impaired fertility and reproductive performance from mupirocin.

iii. Revise the "Pregnancy Category B" subsection as follows:

Pregnancy: Teratogenic Effects: Pregnancy Category B: Reproduction studies have ... and rabbits with mupirocin administered subcutaneously at doses up to 22 and 43 times, respectively, the human topical dose (approximately 60 mg mupirocin per day) on a mg/m^2 basis and revealed no evidence of harm to the fetus due to mupirocin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

iv. Revise the "Nursing Mothers" subsection as follows:

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when mupirocin ointment is administered to a nursing woman.

v. Add the following as the last subsection:

Pediatric Use: The safety and effectiveness of mupirocin ointment have been established in the age range of 2 months to 16 years. Use of mupirocin ointment in these age groups is supported by evidence from adequate and well-controlled studies of mupirocin ointment in impetigo in pediatric patients studied as a part of the pivotal clinical trials (See **CLINICAL STUDIES**)

f. DOSAGE AND ADMINISTRATION

"reevaluated" (delete the [redacted]

g. Add the section below to immediately follow the DOSAGE AND ADMINISTRATION section:

CLINICAL STUDIES

The efficacy of topical mupirocin ointment in impetigo was tested in two studies. In the first, patients with impetigo were randomized to receive either mupirocin ointment or vehicle placebo t.i.d. for 8 to 12 days. Clinical efficacy rates at end of therapy in the evaluable populations (adults and pediatric patients included) were 71% for mupirocin ointment (n=49) and 35% for vehicle placebo (n=51). Pathogen eradication rates in the evaluable populations were 94% for mupirocin ointment and 62% for vehicle placebo. There were no side effects reported in the group receiving mupirocin ointment.

In the second study, patients with impetigo were randomized to receive either mupirocin ointment t.i.d. or 30 to 40 mg/kg oral erythromycin ethylsuccinate per day (this was an unblinded study) for 8 days. There was a follow-up visit 1 week after treatment ended. Clinical efficacy rates at the follow-up visit in the evaluable populations (adults and pediatric patients included) were 93% for mupirovin ointment (n=29) and 78.5% for erythromycin (n=28). Pathogen eradication rates in the evaluable patient populations were 100% for both test groups. There were no side effects reported in the mupirocin ointment group.

Pediatrics: There were 91 pediatric patients aged 2 months to 15 years in the first study described above. Clinical efficacy rates at end of therapy in the evaluable populations were 78% for mupirocin ointment (n=42) and 36% for vehicle placebo (n=49). In the second study described above, all patients were pediatric except two adults in the group receiving mupirocin ointment. The age range of the pediatric patients was 7 months to 13 years. The clinical efficacy rate for mupirocin ointment (n=27) was 96%, and for the erythromycin it was unchanged (78.5%).

h. HOW SUPPLIED

i. See GENERAL COMMENT above.

ii. Add the statement "Bactroban® Nasal is a registered trademark of SmithKline Beecham Pharmaceuticals."

Please revise your container labels and carton and insert labeling, as instructed above, and submit container labels and carton labeling in final print and insert labeling in draft. You may submit insert labeling in final print if you prefer.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes -
http://www.fda.gov/cder/ogd/rld/labeling review branch.html

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.

Wm. Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):
Do you have 12 Final Printed Labels and Labeling? Yes No If no, list why:
Container Labels: 15 gram and 30 gram
Carton Labeling: 1 x 15 gram and 1 x 30 gram
Professional Package Insert Labeling:
Revisions needed post-approval:
BASIS OF APPROVAL:
Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Bactroban® Ointment
NDA Number: 50-591
NDA Drug Name: Bactroban® (mupirocin 2%) Ointment
NDA Firm: SmithKline Beecham
Date of Approval of NDA Insert and supplement #: 4/22/99 (SE8-022)
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-sides
Basis of Approval for the Carton Labeling: side-by-sides
Other Comments:

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 24	X		
Is this name different than that used in the Orange Book?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? No		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	
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? NO Issues for FTR: Innovator individually cartoned? YES Light sensitive product which might require cartoning? NO Must the package insert accompany the product? YES	X	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	
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	
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	
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	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		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.		X	
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. Review based on the labeling of Bactroban® Ointment, approved 4/22/99 in draft (NDA 50-591/SE8-022).

2. Patent/ Exclusivities:

   There are no active patents or exclusivities for this drug product.

3. Storage Conditions:
   NDA – Store between 15° and 30°C (59° and 86°F).
   ANDA – Store at controlled room temperature, between 15° and 30°C (59° and 86°F).
   USP – Preserve in collapsible tubes or in well-closed containers

4. Product Line:
   The innovator markets their product in 1 gram Single Unit Packages of 50 and 15 gram and 30 gram tubes.
   The applicant proposes to market their product in 15 gram and 30 gram tubes.

5. Teva is the manufacturer.

6. Inactive Ingredients:
   The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 60 (Volume 1.1).

7. This is a first generic.

Date of Review: 4-12-01 **Date of Submission:** 1-11-01

Primary Reviewer: Adolph Vezza A. Vezza **Date:** 4/18/01

Team Leader: Charlie Hoppes Charlie Hoppes **Date:** 4/18/01

cc: ANDA: 65-085
DUP/DIVISION FILE
HFD-613/AVezza/CHoppes (no cc)
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Review

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

ANDA Number: 65-085

Date of Submission: October 25, 2001

Applicant's Name: TEVA Pharmaceuticals USA

Established Name: Mupirocin Ointment USP, 2%

Labeling Deficiencies:

1. CARTON 1 x 15 gram and 1 x 30 gram

   a. We encourage you to include an Information for Patient section as seen in your insert labeling.

   b. When printing final printed carton labeling, please ensure that the established name appears on each panel.

2. INSERT

   a. TITLE

      Immediately following the established name add the text, "For Dermatolgic Use".

   b. INDICATIONS AND USAGE

      Revise to read, "Mupirocin ointment 2% is …

   c. PRECAUTIONS

      Revise as follows:

      i. First paragraph –

         … mupirocin ointment 2%, treatment …

      ii. Third paragraph –

         …formulation - *Bactroban® Nasal …
         [Add asterisk].

      iii. Information for Patients

         Revise " ——— to read "health provider. It … health care practitioner…
         [two words instead of one]

d. HOW SUPPLIED

i. We encourage the inclusion of the NDC numbers in this section.

ii. Add an asterisk immediately prior to the statement "*Bactroban® Nasal ...".

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

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes - http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

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.

Wm. Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):
Do you have 12 Final Printed Labels and Labeling? Yes No If no, list why:
Container Labels: 15 gram and 30 gram
Carton Labeling: 1 x 15 gram and 1 x 30 gram
Professional Package Insert Labeling:
Revisions needed post-approval:
BASIS OF APPROVAL: /
Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Bactroban® Ointment
NDA Number: 50-591
NDA Drug Name: Bactroban® (mupirocin 2%) Ointment
NDA Firm: SmithKline Beecham
Date of Approval of NDA Insert and supplement #: 4/22/99 (SE8-022)
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-sides
Basis of Approval for the Carton Labeling: side-by-sides
Other Comments:

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 24	X		
Is this name different than that used in the Orange Book?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? No		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	
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? NO Issues for FTR: Innovator individually cartoned? YES Light sensitive product which might require cartoning? NO Must the package insert accompany the product? YES	X	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	
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	
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	
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	

Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		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.		X	
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:

In the CLINICAL PHARMACOLOGY/Microbiology section the firm indicates that, "Mupircin is an antibacterial agent produced by fermentation using the organism *Pseudomonas fluorescens".*

Is this information accurate for this ANDA?

APPEARS THIS WAY
ON ORIGINAL

FOR THE RECORD: [Portions from previous reviewer].

1. Review based on the labeling of Bactroban® Ointment, approved 4/22/99 in draft (NDA 50-591/SE8-022).

2. Patent/ Exclusivities:

   There are no active patents or exclusivities for this drug product.

3. Storage Conditions:
   NDA – Store between 15° and 30°C (59° and 86°F).
   ANDA – Store at controlled room temperature, between 15° and 30°C (59° and 86°F).
   USP – Preserve in collapsible tubes or in well-closed containers

4. Product Line:
   The innovator markets their product in 1 gram Single Unit Packages of 50 and 15 gram and 30 gram tubes.
   The applicant proposes to market their product in 15 gram and 30 gram tubes.

4. Teva is the manufacturer.

6. Inactive Ingredients:
   The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 60 (Volume 1.1).

7. This is a first generic.

Date of Review: 12/7/01

Date of Submission: 10/25/01

Primary Reviewer: Jacqueline Council, Pharm.D. Date: 12-17-01

Charlie Hoppes, Team Leader Date: 12/18/01

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cc: ANDA: 65-085
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Review

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

ANDA Number: 65-085

Date of Submission: August 23, 2002

Applicant's Name: TEVA Pharmaceuticals USA

Established Name: Mupirocin Ointment USP, 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: 15 gram and 30 gram
Satisfactory in FPL as of the August 23, 2002 submission, [Vol. 4.1, Attachment 6]

Carton Labeling: 1 x 15 gram and 1 x 30 gram
Satisfactory in FPL as of the August 23, 2002 submission, [Vol. 4.1, Attachment 6]

Professional Package Insert Labeling:
Satisfactory in FPL as of the August 23, 2002 submission, [Vol. 4.1, Attachment 6, Iss. 8/2002, Code I20738]

Revisions needed post-approval: None

BASIS OF APPROVAL:

Patent Data – NDA 50-591

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data– NDA 50-591

Code	Reference	Expiration	Labeling Impact
None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Bactroban® Ointment
NDA Number: 50-591
NDA Drug Name: Bactroban® (mupirocin 2%) Ointment
NDA Firm: SmithKline Beecham
Date of Approval of NDA Insert and supplement #: 4/22/99 (SE8-022)
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-sides
Basis of Approval for the Carton Labeling: side-by-sides
Other Comments:

APPEARS THIS WAY
ON ORIGINAL

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 25	X		
Is this name different than that used in the Orange Book?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? No		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	
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? NO Issues for FTR: Innovator individually cartoned? YES Light sensitive product which might require cartoning? NO Must the package insert accompany the product? YES	X	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	
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	
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	
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	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		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.		X	
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:

In the CLINICAL PHARMACOLOGY/Microbiology section the firm indicates that, "Mupirocin is an antibacterial agent produced by fermentation using the organism *Pseudomonas fluorescens".*

Is this information accurate for this ANDA?

Yes, Mupirocin is an antibacterial agent produced by fermentation using the organism *Pseudomonas fluorescens.* This is an accurate statement.
Scott

FOR THE RECORD: [Portions from previous reviewer].

1. Review based on the labeling of Bactroban® Ointment (NDA 50-591/SE8-022) approved 4/22/99 in draft; issued 5/99).

2. Storage Conditions:
NDA – Store at controlled room temperature 20° to 25° C (68° to 77°F).
ANDA – Store at controlled room temperature between 15° and 30°C (59° and 86°F)(see USP).
USP – Preserve in collapsible tubes or in well-closed containers

3. Product Line:
The innovator markets their product in 1 gram Single Unit Packages of 50 and 15 gram and 30 gram tubes.
The applicant proposes to market their product in 15 gram and 30 gram tubes.

4. Teva is the manufacturer.

5. Inactive Ingredients:
The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 60 (Volume 1.1).

6. This is a first generic.

Date of Review: 09/30/02 Date of Submission: 8/23/02

Primary Reviewer: Michelle Dillahunt MDillahunt Date: 10/1/02

Team Leader: Lillie Golson LGolson Date: 10/1/02

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cc: ANDA: 65-085
DUP/DIVISION FILE
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Review

APPEARS THIS WAY
ON ORIGINAL

SUPERSEDES APPROVAL SUMMARY FOR SUBMISSION DATED AUGUST 23, 2002
APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 65-085

Date of Submission: April 14, 2003

Applicant's Name: TEVA Pharmaceuticals USA

Established Name: Mupirocin Ointment USP, 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: 15 gram, 22 gram and 30 gram

Satisfactory in FPL as of the August 23, 2002 submission, [Vol. 4.1, Attachment 6] –15 gram and 30 gram

Satisfactory in FPL as of the April 14, 2003 submission [Vol. 5.1, Attachment 7]- 22 gram

Carton Labeling: 1 x 15 gram, 1 x 22 gram and 1 x 30 gram

Satisfactory in FPL as of the August 23, 2002 submission, [Vol. 4.1, Attachment 6]- 15 gram and 30 gram

Satisfactory in FPL as of the April 14, 2003 submission [Vol. 5.1, Attachment 7]- 22 gram

Professional Package Insert Labeling:

Satisfactory in FPL as of the April 14, 2003 submission, [Vol. 5.1, Attachment 7, Rev. D 4/2003].

Revisions needed post-approval:
GENERAL: Revise your storage temperature on your container labels and insert labeling to:
Store at 20-25° C (68 - 77 ° F)
[see USP Controlled Room Temperature]
The firm has submitted a commitment to revise the labeling storage conditions as stated above at time of next printing. (see correspondence dated 6/17/03)

BASIS OF APPROVAL:

Patent Data – NDA 50-591

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data– NDA 50-591

Code	Reference	Expiration	Labeling Impact
None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Bactroban® Ointment
NDA Number: 50-591
NDA Drug Name: Bactroban® (mupirocin 2%) Ointment
NDA Firm: SmithKline Beecham
Date of Approval of NDA Insert and supplement #: 4/22/99 (SE8-022)
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-sides
Basis of Approval for the Carton Labeling: side-by-sides
Other Comments:

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 26	X		
Is this name different than that used in the Orange Book?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? No		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	
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? NO Issues for FTR: Innovator individually cartoned? YES Light sensitive product which might require cartoning? NO Must the package insert accompany the product? YES	X	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	
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	
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	
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	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		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.		X	
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:

In the CLINICAL PHARMACOLOGY/Microbiology section the firm indicates that, "Mupirocin is an antibacterial agent produced by fermentation using the organism *Pseudomonas fluorescens*".

Is this information accurate for this ANDA?

Yes, Mupirocin is an antibacterial agent produced by fermentation using the organism *Pseudomonas fluorescens*. This is an accurate statement.
Scott

FOR THE RECORD: [Portions from previous reviewer].

1. Review based on the labeling of Bactroban® Ointment (NDA 50-591/SE8-022) approved 4/22/99 in draft; issued 5/99).

2. Storage Conditions:
NDA – Store at controlled room temperature 20° to 25° C (68° to 77°F).
ANDA – Store at controlled room temperature between 15° and 30°C (59° and 86°F)(see USP).
USP – Preserve in collapsible tubes or in well-closed containers
The firm provided a commitment to revise storage temperature to: 20° to 25° C (68° to 77°F) [see USP Controlled Room Temperature]

3. Product Line:
The innovator markets their product in 1 gram Single Unit Packages of 50 and 15 gram and 30 gram tubes.
The applicant proposes to market their product in 15 gram, 22 gram and 30 gram tubes.

4. Teva submitted an amendment on April 14, 2003 to add a 22 gram package size

5. Teva is the manufacturer.

6. Inactive Ingredients:
The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on page 60 (Volume 1.1).

7. This is a first generic.

Date of Review: 6/23/03

Date of Submission: 4/14/03

Primary Reviewer: Michelle Dillahunt

Date: 6/24/03

Team Leader: Lillie Golson

Date: 6/24/03

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cc: ANDA: 65-085
DUP/DIVISION FILE
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Review

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-085

CHEMISTRY REVIEW(S)

ANDA APPROVAL SUMMARY

ANDA: 65-085

DRUG PRODUCT: Mupirocin Ointment USP

FIRM: TEVA Pharmaceuticals USA

DOSAGE FORM: Ointment

POTENCY: 2%

CGMP STATEMENT/EER UPDATE STATUS: Signed cGMP certification was provided on p. 2575 of the original submission. EER was found acceptable on 6/18/01.

BIO STUDY: The Bio Study was found acceptable by the Medical Officer on 01-MAR-2002. The Biostatistical consult was found acceptable on 1/7/03.

METHODS VALIDATION – (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S): The drug substance and drug product are both USP. The firm is using the USP testing methods with the following exception: they are using a ——— assay method for the non-compendial test of Related Compounds and Impurities. Appropriate validation data were provided.

STABILITY – (ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION?): Containers used in the stability studies were identical to those described in the container section. An 18-month expiration date has been established for this strength of drug product. See Stability Section of Review for a thorough explanation of this truncated expiry.

LABELING: Labeling was approved on 6/24/03.

STERILIZATION VALIDATION (IF APPLICABLE): N/A

SIZE OF BIO BATCH (FIRM'S SOURCE OF NDS OK?): The exhibit batch records were included for lot #0984-034 for a batch size of ——— of drug product. Master batch records were provided for the projected market batch size of ——— of drug product. The manufacturing process described in the executed batch records is the same as that provided in the master batch records. The firm proposed addition of a new package size of 22 grams in the 4/14/03 amendment. In addition to this new packaging size added

in that amendment, the firm also proposes a scale-up to ——— from the original batch size of ——— In support of these changes, the firm provided copies of executed batch records (lot #1454-066) in Attachment 2 of the 4/14/03 submission. This batch was packaged into 15 gram, 22 gram, and 30 gram tubes. A proposed commercial product batch record was provided in Attachment 6 of the 4/14/03 submission. The — drug substance was obtained from ———

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH, WERE THEY MANUFACTURED VIA THE SAME PROCESS?): See above

PROPOSED PRODUCTION BATCH - (MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?): See Above.

CHEMIST: SCOTT FURNESS **DATE:** 9/15/03 10/2/03

SUPERVISOR: RICHARD ADAMS **DATE:** R.C. Adams 10/3/03

APPEARS THIS WAY
ON ORIGINAL

1. CHEMISTRY REVIEW NO. 1

2. ANDA # 65-085

3. NAME AND ADDRESS OF APPLICANT
TEVA Pharmaceuticals USA
Agent: Vincent Andolina
1090 Horsham Road
P.O. Box 1090
North Wales, PA 19454

4. LEGAL BASIS FOR SUBMISSION
Reference Listed drug product: Bactroban® Ointment by Smithkline Beecham approved in NDA #50-591. The firm filed a patent certification exemption statement indicating that the RLD is subject to the exception provision of section 125 (d)(2) of Title 1 of FDAMA. As such, certification to the listed patents is not required. (p. 9). No exclusivities noted (p. 10). The proposed drug product contains the same active ingredient and has the same strength, dosage form, route of administration, indication, and usage as the reference listed drug.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Mupirocin Ointment USP, 2%

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

Firm	Original Submission:	11-JAN-2001
	Telephone Amendment:	13-FEB-2001
FDA	Acceptable for Filing:	21-FEB-2001

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. Rx or OTC
Rx

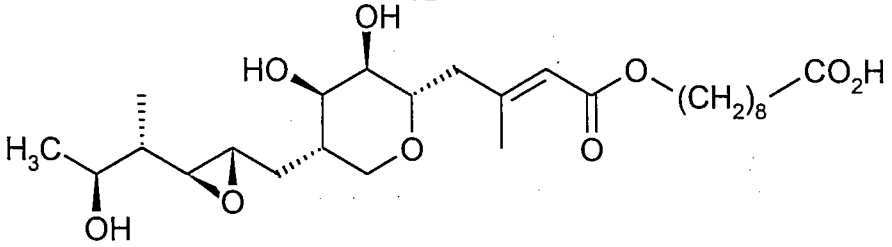
12. RELATED IND/NDA/DMF(s)
DMF

DMF ——— [redacted]

13. DOSAGE FORM
Ointment

14. POTENCY
2%

15. CHEMICAL NAME AND STRUCTURE



Chemical Name: (E)-(2S,3R,4R,5S)-5-[(2S,3S,4S,5S)-2,3-Epoxy-5-hydroxy-4-methylhexyl]tetrahydro-3,4-dihydroxy-b-methyl-2H-pyran-2-crotonic acid, ester with 9-hydroxynonanoic acid [12650-69-0]
Molecular Weight: 500.62

16. RECORDS AND REPORTS
N/A

17. COMMENTS
This first cycle submission contains minor deficiencies with respect to CMC. The Bioequivalency Studies, Labeling studies and EER remain pending. Methods validation will not be necessary since both the drug substance and drug product are compendial.

18. CONCLUSIONS AND RECOMMENDATIONS
Not-Approvable (MINOR)

19. REVIEWER: M. Scott Furness

DATE COMPLETED: 4/17/01

Redacted 14

Page(s) of trade secret and /or confidential commercial information

1. CHEMISTRY REVIEW NO. 2

2. ANDA # 65-085

3. NAME AND ADDRESS OF APPLICANT
TEVA Pharmaceuticals USA
Agent: Vincent Andolina
1090 Horsham Road
P.O. Box 1090
North Wales, PA 19454

4. LEGAL BASIS FOR SUBMISSION
Reference Listed drug product: Bactroban® Ointment by Smithkline Beecham approved in NDA #50-591. The firm filed a patent certification exemption statement indicating that the RLD is subject to the exception provision of section 125 (d)(2) of Title 1 of FDAMA. As such, certification to the listed patents is not required. (p. 9). No exclusivities noted (p. 10). The proposed drug product contains the same active ingredient and has the same strength, dosage form, route of administration, indication, and usage as the reference listed drug.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Mupirocin Ointment USP, 2%

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

Firm	Original Submission:	11-JAN-2001
	Telephone Amendment:	13-FEB-2001
	CMC/Labeling Amendment:	25-OCT-2001
FDA	Acceptable for Filing:	21-FEB-2001
	Labeling Deficiency:	18-APR-2001

10. PHARMACOLOGICAL CATEGORY
Antibacterial

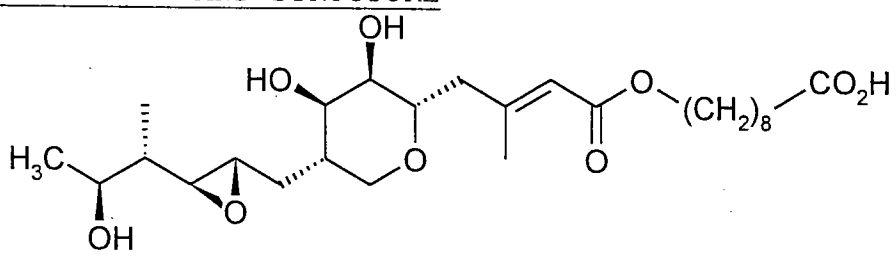
11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)
DMF [redacted]
DMF [redacted]

13. DOSAGE FORM
Ointment

14. POTENCY
2%

15. CHEMICAL NAME AND STRUCTURE



Chemical Name: (E)-(2S,3R,4R,5S)-5-[(2S,3S,4S,5S)-2,3-Epoxy-5-hydroxy-4-methylhexyl]tetrahydro-3,4-dihydroxy-b-methyl-2H-pyran-2-crotonic acid, ester with 9-hydroxynonanoic acid [12650-69-0]
Molecular Weight: 500.62

16. RECORDS AND REPORTS
N/A

17. COMMENTS
This second cycle submission contains minor deficiencies with respect to CMC. The Bioequivalency Studies remain pending. Labeling remains deficient. EER was found acceptable on 6/18/01. Methods validation will not be necessary since both the drug substance and drug product are compendial.

18. CONCLUSIONS AND RECOMMENDATIONS
Not-Approvable (MINOR)

19. REVIEWER: M. Scott Furness
DATE COMPLETED: 12/11/01

Redacted 17

Page(s) of trade secret and /or confidential commercial information

1. CHEMISTRY REVIEW NO. 3

2. ANDA # 65-085

3. NAME AND ADDRESS OF APPLICANT
TEVA Pharmaceuticals USA
Agent: Vincent Andolina
1090 Horsham Road
P.O. Box 1090
North Wales, PA 19454

4. LEGAL BASIS FOR SUBMISSION
Reference Listed drug product: Bactroban® Ointment by Smithkline Beecham approved in NDA #50-591. The firm filed a patent certification exemption statement indicating that the RLD is subject to the exception provision of section 125 (d)(2) of Title 1 of FDAMA. As such, certification to the listed patents is not required. (p. 9). No exclusivities noted (p. 10). The proposed drug product contains the same active ingredient and has the same strength, dosage form, route of administration, indication, and usage as the reference listed drug.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Mupirocin Ointment USP, 2%

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

Firm	Original Submission:	11-JAN-2001
	Telephone Amendment:	13-FEB-2001
	CMC/Labeling Amendment:	25-OCT-2001
	Bioequivalency Amendment:	21-JAN-2002
	CMC Amendment:	15-APR-2002
FDA	Acceptable for Filing:	21-FEB-2001
	Labeling Deficiency #1:	18-APR-2001
	CMC Deficiency #1:	26-APR-2001
	Medical Officer Deficiency:	26-NOV-2001
	Bioequivalency Deficiency:	05-DEC-2001
	Labeling Deficiency #2:	18-DEC-2001
	CMC Deficiency #2:	14-JAN-2002

Medical Officer Acceptance: 01-MAR-2002

10. PHARMACOLOGICAL CATEGORY
Antibacterial

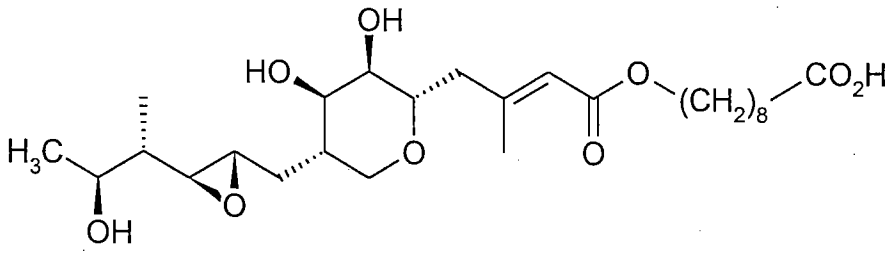
11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)
DMF [redacted]
DMF [redacted]

13. DOSAGE FORM
Ointment

14. POTENCY
2%

15. CHEMICAL NAME AND STRUCTURE



Chemical Name: (E)-(2S,3R,4R,5S)-5-[(2S,3S,4S,5S)-2,3-Epoxy-5-hydroxy-4-methylhexyl]tetrahydro-3,4-dihydroxy-b-methyl-2H-pyran-2-crotonic acid, ester with 9-hydroxynonanoic acid [12650-69-0]
Molecular Weight: 500.62

16. RECORDS AND REPORTS
N/A

17. COMMENTS
This third cycle submission contains minor deficiencies with respect to CMC. The Bioequivalency Studies remain pending. Labeling remains deficient. EER was found acceptable on 6/18/01. Methods validation will not be necessary since both the drug substance and drug product are compendial.

18. CONCLUSIONS AND RECOMMENDATIONS
Not-Approvable (MINOR)

19. REVIEWER:
M. Scott Furness

DATE COMPLETED:
7/26/02

Redacted 18

Page(s) of trade secret and /or confidential commercial information

1. CHEMISTRY REVIEW NO. 4

2. ANDA # 65-085

3. NAME AND ADDRESS OF APPLICANT
TEVA Pharmaceuticals USA
Agent: Vincent Andolina
1090 Horsham Road
P.O. Box 1090
North Wales, PA 19454

4. LEGAL BASIS FOR SUBMISSION
Reference Listed drug product: Bactroban® Ointment by Smithkline Beecham approved in NDA #50-591. The firm filed a patent certification exemption statement indicating that the RLD is subject to the exception provision of section 125 (d)(2) of Title 1 of FDAMA. As such, certification to the listed patents is not required. (p. 9). No exclusivities noted (p. 10). The proposed drug product contains the same active ingredient and has the same strength, dosage form, route of administration, indication, and usage as the reference listed drug.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Mupirocin Ointment USP, 2%

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

Firm	Original Submission:	11-JAN-2001
	Telephone Amendment:	13-FEB-2001
	CMC/Labeling Amendment:	25-OCT-2001
	Bioequivalency Amendment:	21-JAN-2002
	CMC Amendment:	15-APR-2002
	CMC Amendment:	23-AUG-2002
FDA	Acceptable for Filing:	21-FEB-2001
	Labeling Deficiency #1:	18-APR-2001
	CMC Deficiency #1:	26-APR-2001
	Medical Officer Deficiency:	26-NOV-2001
	Bioequivalency Deficiency:	05-DEC-2001
	Labeling Deficiency #2:	18-DEC-2001

CMC Deficiency #2:	14-JAN-2002
CMC Deficiency #3:	01-AUG-2002
Labeling Deficiency #3:	01-AUG-2002
Medical Officer Acceptance:	01-MAR-2002
Biostatistical Acceptance:	07-JAN-2003
Labeling Acceptance:	*01-OCT-2002*

10. PHARMACOLOGICAL CATEGORY
Antibacterial

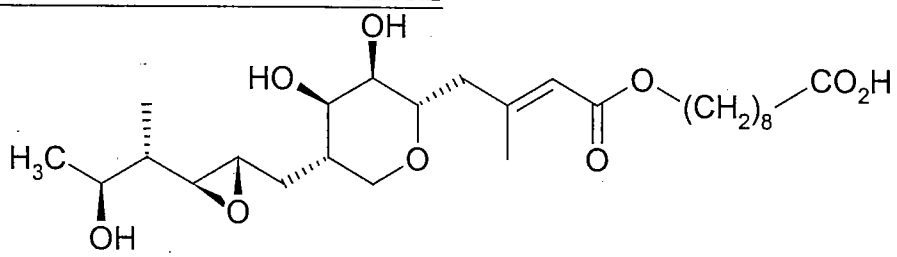
11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)
DMF [redacted]
DMF [redacted]

13. DOSAGE FORM
Ointment

14. POTENCY
2%

15. CHEMICAL NAME AND STRUCTURE



Chemical Name: (E)-(2S,3R,4R,5S)-5-[(2S,3S,4S,5S)-2,3-Epoxy-5-hydroxy-4-methylhexyl]tetrahydro-3,4-dihydroxy-b-methyl-2H-pyran-2-crotonic acid, ester with 9-hydroxynonanoic acid [12650-69-0]
Molecular Weight: 500.62

16. RECORDS AND REPORTS
N/A

17. COMMENTS
This fourth cycle submission successfully addressed all deficiencies with respect to CMC. The Bioequivalency Studies, Labeling, and EER were found acceptable. Methods validation will not be necessary since both the drug substance and drug product are compendial.

18. CONCLUSIONS AND RECOMMENDATIONS
Approval is recommended.

19. REVIEWER: M. Scott Furness

DATE COMPLETED: 9/4/02

APPEARS THIS WAY
ON ORIGINAL

Redacted 15

Page(s) of trade secret and /or confidential commercial information

1. CHEMISTRY REVIEW NO. 5

2. ANDA # 65-085

3. NAME AND ADDRESS OF APPLICANT
TEVA Pharmaceuticals USA
Agent: Vincent Andolina
1090 Horsham Road
P.O. Box 1090
North Wales, PA 19454

4. LEGAL BASIS FOR SUBMISSION
Reference Listed drug product: Bactroban® Ointment by Smithkline Beecham approved in NDA #50-591. The firm filed a patent certification exemption statement indicating that the RLD is subject to the exception provision of section 125 (d)(2) of Title 1 of FDAMA. As such, certification to the listed patents is not required. (p. 9). No exclusivities noted (p. 10). The proposed drug product contains the same active ingredient and has the same strength, dosage form, route of administration, indication, and usage as the reference listed drug.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Mupirocin Ointment USP, 2%

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

Firm	Original Submission:	11-JAN-2001
	Telephone Amendment:	13-FEB-2001
	CMC/Labeling Amendment:	25-OCT-2001
	Bioequivalency Amendment:	21-JAN-2002
	CMC Amendment:	15-APR-2002
	CMC Amendment:	23-AUG-2002
	Unsolicited Amendment:	14-APR-2003
FDA	Acceptable for Filing:	21-FEB-2001
	Labeling Deficiency #1:	18-APR-2001
	CMC Deficiency #1:	26-APR-2001
	Medical Officer Deficiency:	26-NOV-2001
	Bioequivalency Deficiency:	05-DEC-2001

Labeling Deficiency #2:	18-DEC-2001
CMC Deficiency #2:	14-JAN-2002
CMC Deficiency #3:	01-AUG-2002
Labeling Deficiency #3:	01-AUG-2002
Medical Officer Acceptance:	01-MAR-2002
Biostatistical Acceptance:	07-JAN-2003
Labeling Acceptance:	14-APR-2003

10. PHARMACOLOGICAL CATEGORY
Antibacterial

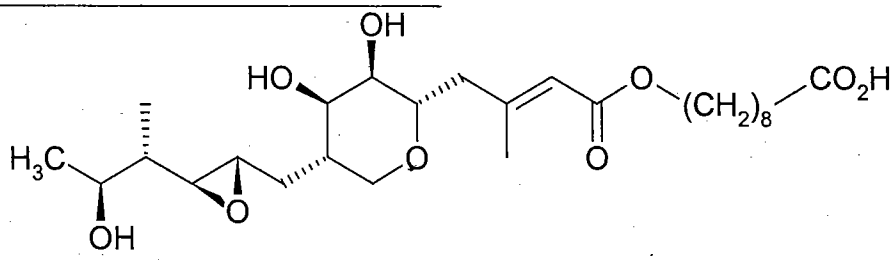
11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)
DMF [redacted]
DMF [redacted]

13. DOSAGE FORM
Ointment

14. POTENCY
2%

15. CHEMICAL NAME AND STRUCTURE



Chemical Name: (E)-(2S,3R,4R,5S)-5-[(2S,3S,4S,5S)-2,3-Epoxy-5-hydroxy-4-methylhexyl]tetrahydro-3,4-dihydroxy-b-methyl-2H-pyran-2-crotonic acid, ester with 9-hydroxynonanoic acid [12650-69-0]
Molecular Weight: 500.62

16. RECORDS AND REPORTS
N/A

17. COMMENTS
Although the fourth cycle CMC submission had successfully addressed all deficiencies with respect to CMC, the firm submitted an unsolicited amendment on 4/14/03 for addition of a new 22 gram packaging size. Although the requisite data provided by the applicant to justify that addition is acceptable, the drug substance DMF has been found

inadequate. The Bioequivalency Studies, Labeling, and EER were found acceptable. Methods validation will not be necessary since both the drug substance and drug product are compendial.

18. CONCLUSIONS AND RECOMMENDATIONS
Not-Approvable (MINOR)

19. REVIEWER:
M. Scott Furness

DATE COMPLETED:
7/29/03

APPEARS THIS WAY
ON ORIGINAL

Redacted 20

Page(s) of trade secret and /or confidential commercial information

1. CHEMISTRY REVIEW NO. 6

2. ANDA # 65-085

3. NAME AND ADDRESS OF APPLICANT
TEVA Pharmaceuticals USA
Agent: Vincent Andolina
1090 Horsham Road
P.O. Box 1090
North Wales, PA 19454

4. LEGAL BASIS FOR SUBMISSION
Reference Listed drug product: Bactroban® Ointment by Smithkline Beecham approved in NDA #50-591. The firm filed a patent certification exemption statement indicating that the RLD is subject to the exception provision of section 125 (d)(2) of Title 1 of FDAMA. As such, certification to the listed patents is not required. (p. 9). No exclusivities noted (p. 10). The proposed drug product contains the same active ingredient and has the same strength, dosage form, route of administration, indication, and usage as the reference listed drug.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Mupirocin Ointment USP, 2%

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

Firm	Original Submission:	11-JAN-2001
	Telephone Amendment:	13-FEB-2001
	CMC/Labeling Amendment:	25-OCT-2001
	Bioequivalency Amendment:	21-JAN-2002
	CMC Amendment:	15-APR-2002
	CMC Amendment:	23-AUG-2002
	Unsolicited Amendment:	14-APR-2003
	CMC Amendment:	13-AUG-2003
FDA	Acceptable for Filing:	21-FEB-2001
	Labeling Deficiency #1:	18-APR-2001
	CMC Deficiency:	26-APR-2001
	Medical Officer Deficiency:	26-NOV-2001

Bioequivalency Deficiency:	05-DEC-2001
Labeling Deficiency #2:	18-DEC-2001
CMC Deficiency:	14-JAN-2002
CMC Deficiency:	01-AUG-2002
Labeling Deficiency #3:	01-AUG-2002
Medical Officer Acceptance:	01-MAR-2002
Biostatistical Acceptance:	07-JAN-2003
Labeling Acceptance:	14-APR-2003
CMC Deficiency:	05-AUG-2003

10. PHARMACOLOGICAL CATEGORY
Antibacterial

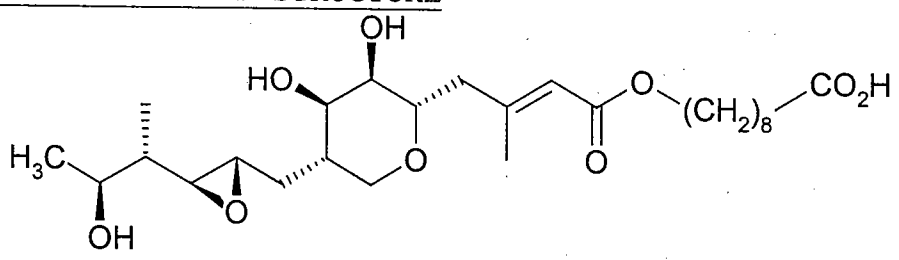
11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)
DMF [redacted]
DMF [redacted]

13. DOSAGE FORM
Ointment

14. POTENCY
2%

15. CHEMICAL NAME AND STRUCTURE



Chemical Name: (E)-(2S,3R,4R,5S)-5-[(2S,3S,4S,5S)-2,3-Epoxy-5-hydroxy-4-methylhexyl]tetrahydro-3,4-dihydroxy-b-methyl-2H-pyran-2-crotonic acid, ester with 9-hydroxynonanoic acid [12650-69-0]
Molecular Weight: 500.62

16. RECORDS AND REPORTS
N/A

17. COMMENTS
This sixth cycle submission successfully addressed all deficiencies with respect to CMC. The Bioequivalency Studies, Labeling, and EER were found acceptable. Methods

validation will not be necessary since both the drug substance and drug product are compendial.

18. CONCLUSIONS AND RECOMMENDATIONS
Approval is recommended.

19. REVIEWER: M. Scott Furness

DATE COMPLETED: 9/15/03

APPEARS THIS WAY
ON ORIGINAL

Redacted 19

Page(s) of trade secret and /or confidential commercial information

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-085

BIOEQUIVALENCE REVIEW(S)

1.1 Ack. mark

DEC - 5 2001

BIOEQUIVALENCY DEFICIENCIES

ANDA: # 65-085 APPLICANT: TEVA Pharmaceuticals USA

DRUG PRODUCT: Mupirocin Ointment USP, 2%

The Division of Bioequivalence has completed its review of your submission(s) acknowledged on the cover sheet. The following deficiencies have been identified:

1. You have not provided specific details regarding how the independent audit of the tubes with packaging problems was carried out.

2. All patients who received study medication prior to correction of the packaging problem that led to potential unblinding (i.e., July 1, 2000) should be excluded from the study analysis. Please reanalyze the data excluding these patients and submit the reanalysis to the Agency.

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:

65-085

CORRESPONDENCE

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 8642
FAX: (215) 591 8812

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

August 13, 2003

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NF[illegible] [illegible]E
[illegible]

N\Am
RECEIVED
AUG 1 4 2003
OGD/CDER

ANDA #65-085
MUPIROCIN OINTMENT USP, 2%
NEW CORRESPONDENCE

Dear Mr. Buehler:

Teva Pharmaceuticals USA submits herewith information to the above-referenced ANDA in response to a letter from the Office of Generic Drugs dated August 5, 2003 (provided in **Attachment 1** for ease of review). The August 5, 2003 letter contains a single comment, namely that [redacted] DMF [redacted] for [redacted] was found deficient.

[redacted] was issued a deficiency letter based on an update they submitted to their DMF in May 2003. Please note that [redacted] May 2003 submission contained no substantive changes, and as such, they have requested withdrawal of the submission. A copy of [redacted] August 8, 2003 request for withdrawal of the submission is enclosed in **Attachment 2** for your reference.

As DMF [redacted] should require no further review at this time, we believe there are no outstanding deficiencies remaining for ANDA #65-085. Therefore, we look forward to final approval of this application. Should you have any further questions or comments, please feel free to contact me at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

Vincent Andolina

VA/jbp
Enclosures

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 8642
FAX: (215) 591 8812

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

June 17, 2003

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

TELEPHONE AMENDMENT

NEW CORRESP
NC

ANDA #65-085
MUPIROCIN OINTMENT USP, 2%
TELEPHONE AMENDMENT- RESPONSE TO JUNE 13, 2003 REQUEST

Dear Mr. Buehler:

Teva Pharmaceuticals USA submits herewith a telephone amendment to the above-referenced ANDA in response to a telephone request received on June 13, 2003 in a conversation between Michelle Dillahunt of the Office of Generic Drugs and Philip Erickson, Director of Regulatory Affairs at Teva. During this conversation Ms. Dillahunt requested a commitment for the revision of the labeled storage condition for the packaged drug product to indicate storage between 20° - 25° C (68° and 77° F). Please note that this application was originally submitted on January 11, 2001 with our current labeled storage requirement of " Store at controlled room temperature 15° to 30°C (59° to 86°F) (see USP)". The original application proposed packaging in 15 gram and 30 gram tubes and was amended on April 14, 2003 to propose a commercial package size of 22 gram tubes. The labeling proposed throughout this pending application has always contained our stated range of 15° to 30° C.

In the absence of any previous comment regarding the stated storage temperature, Teva has manufactured and packaged [redacted] validation batches in preprinted tubes that contain reference to our original storage statement. The stability data provided in relation to all package sizes contained in this application were deemed supportive of the labeled storage conditions. Furthermore, the USP definition of controlled room temperature allows for excursions within the temperature range stated by our labeling and appropriate reference to USP storage is provided within the storage statement text.

RECEIVED
JUN 18 2003
OGD / CDER

As the difference in storage statement does not pose an issue of product quality, Teva proposes to initially market the — validation batches of drug product with the original storage statement proposed by this application. This proposal will avoid the unnecessary destruction of drug product as it is not possible to repackage a semi-solid drug product, nor is it feasible to over label the tubes. We hereby commit to immediately update the storage statement to the requested 20° to 25°C (68° to 77°F) temperature range on all affected labeling for this product. The revised labeling will be provided to this application as a post approval Special Supplement – Changes Being Effected in 0 days. Teva further commits that all product manufactured from this point forward will be packaged with the requested storage temperature statement. This proposal was discussed and deemed acceptable by Mark Anderson of your office in a June 16, 2003 telephone conversation.

It is our belief that the information provided herein represents a complete response to the request set forth in the June 13, 2003 telephone request. We look forward to final approval of ANDA 65-085. Should you have any further questions or comments, please feel free to contact me at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

VA/rsv
Enclosures

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 8642
FAX: (215) 591 8812

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

April 14, 2003

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

UNSOLICITED AMENDMENT:
ADDITION OF 22 GRAM
PACKAGE SIZE

ORIG AMENDMENT
N/AC

ANDA #65-085
MUPIROCIN OINTMENT USP, 2%
UNSOLICITED AMENDMENT- ADDITION OF 22 GRAM PACKAGE SIZE

Dear Mr. Buehler:

Teva Pharmaceuticals USA submits herewith an unsolicited amendment to the above-referenced ANDA with the purpose of proposing a 22 gram package size for Mupirocin Ointment USP, 2%. Please note that on July 22, 2002, Vincent Andolina of TEVA Pharmaceuticals USA discussed this change with Mark Anderson of the Office of Generic Drugs who confirmed that use of the CBE-30 filing mechanism was appropriate should this change be made post-approval. In light of the recent Citizen Petition filed by GlaxoSmithKline requesting delay of approval of generic Mupirocin Ointment ANDAs, TEVA is submitting this proposal prior to final approval of ANDA 65-085.

This proposal is being made as it has come to our attention that the innovator company has ceased marketing 15 gram and 30 gram package sizes, and now only markets in a 22 gram package configuration.

In addition to the new package size, the exhibit batch and the proposed commercial manufacturing directions contained herein also contain a batch size scale-up to [redacted], from the original batch size of [redacted] In accord with SUPAC Guidance for Industry- Nonsterile Semisolid Dosage Forms, section V.A.1, this change is a Level 1 change and as such would be a post-approval annual reportable change. Please note the only equipment change made as a result of this scale change is the use of [redacted]. Specifically, a [redacted]

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In support of our proposal, please find enclosed the following documentation:

Attachment 1: A packaging component summary describing the 22 gram blind end tube and cap is provided. Please note that this packaging component is manufactured by [redacted], and is identical to the 15 and 30 gram tubes approved in ANDA 65-085, with the exception of its dimensions as well as the resin used in manufacture of the cap. In addition, please find a letter of DMF authorization from [redacted] echnical information and diagram of the component, a letter from [redacted] stating that the new cap [redacted], has been used to package other CDER-approved products, and TEVA's packaging component specification sheet. Further, please find a certificate of analysis and a certificate of compliance for this component in Attachment 1.

Attachment 2: An executed batch card is provided for Lot 1454-066 which was packaged in the 15 gram, 22 gram and 30 gram tubes. A packaging and disbursement summary for this batch is also enclosed. Please note that our intent is to package future batches in only the 22 gram configuration.

Attachment 3: A summary of the lot numbers of raw materials used to manufacture Lot 1454-066 are provided in addition to certificates of analysis (TEVA and supplier) for these lots.

Attachment 4: Finished product certificates of analysis are provided for Lot 1454-066 for the 15 gram, 22 gram and 30 gram package sizes.

Attachment 5: Stability summary reports for Lot 1454-066 stored under controlled room temperature and accelerated conditions are provided. Please note that we propose retention of the 18-month shelf life proposed in an August 23, 2002 minor amendment.

Attachment 6: A proposed commercial product batch record updated to reflect the newly proposed 22 gram package size is provided. Please note that TEVA intends to market only the proposed 22 gram package, as this is the only size being marketed by the innovator.

Attachment 7: Twelve copies of final print container labels and carton labels for the 22 gram package size are provided. Please note that these documents are identical to those previously submitted for the 15 gram and 30 gram tubes other than fill size. In addition, twelve copies of final print insert labeling are provided herein. The only change made to this insert is the addition of the 22 gram package to the "how supplied" section. Because it is TEVA's intent to market only the 22 gram package, the insert will be updated post-approval to reflect only the availability of that size.

Should you have any questions or comments regarding the information contained herein, please feel free to contact me at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

Vincent Andolina

VA/jbp
Enclosures

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 8642
FAX: (215) 591 8812

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

ORIG AMENDMENT
N/A6

November 21, 2002

BIOEQUIVALENCE AMENDMENT

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ANDA #65-085
MUPIROCIN OINTMENT USP, 2%
BIOEQUIVALENCE AMENDMENT- RESPONSE TO OCTOBER 24, 2002 TELEPHONE REQUEST

Dear Mr. Buehler:

We submit herewith a bioequivalence amendment to the above-referenced pending ANDA in response to a telephone request received from the Office of Generic Drugs, Division of Medical Affairs on October 24, 2002 via conference call. Participants in the October 24, 2002 discussion included Dr. Dena Hixon, Dr. Krista Scardina, Carol Kim and Dr. H. Li of OGD and Deborah Jaskot, Paul Fackler, Vincent Andolina, David Kormann, and Jill Pastore of TEVA Pharmaceuticals USA. In addition to the call, Dr. Hixon forwarded the comments regarding our application via facsimile, a copy of which is provided in **Attachment 1** for reference.

Please note that a request was placed with Dr. Scardina to allow an extension of the deadline of our response due to the fact that the statistician who originally did the analyses for this study now works for a competitor and therefore can no longer assist us with this project. A new statistician was contracted to perform the re-analyses requested in Dr. Hixon's October 24, 2002 facsimile, so additional time was needed to allow that person to familiarize themselves with the study and the work required.

Comments are addressed below in the order they were presented in the October 24, 2002 facsimile.

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1. A data set consisting of line listings for the 201 patients enrolled in the study on July 1, 2000 or later containing all the information for each patient as requested in comment #1 is provided on compact disc (hereafter "CD") in **Attachment 2.**

2. A listing of all subjects excluded from the Per Protocol (hereafter "PP") or Intent to Treat (hereafter "ITT") population with detailed explanations of the reason for exclusion is provided on the CD in **Attachment 2.**

3. Regarding the different clinical responses between ClinResp and ClinRes2 for some patients, please note that we have reviewed our previous submissions to identify the cause of this possible discrepancy.

   On April 9, 2002 a bioequivalence amendment was sent in response to a March 27, 2002 telephone request. This amendment included a CD that contained output listings and a document file containing a description of each data set and an explanation of variables used for the study. No data sets were sent with this amendment. On May 3, 2002, a bioequivalence amendment was sent in response to an April 22, 2002 telephone request. This amendment included a CD that contained the raw data set of clinical responses (Clinresp).

   To clarify, there are two data sets containing clinical responses, Clinresp and Clinres2. Clinresp contains the raw data while Clinres2 is a derived data set. There were 625 records in the raw data set, Clinresp, and 692 records in the derived data set Clinres2. In Clinres2, 67 records were added to the raw data set according to the nine rules of assigning missing values for clinical response, as described in Section 15.0, page 113 of the Clinical Study Report in the original ANDA. Forty-eight records of clinical response were changed according to the nine rules for assigning clinical response in derived data set Clinres2. There were a total of 38 patients (48 records) that had different clinical responses on the raw data set versus the derived data set. We hope this clarifies the situation, and apologize for any confusion our previous presentations may have caused.

4. Per your request, any patient with a clinical response of "unevaluable" has been excluded from the PP population.

5. As requested, we have included the statistical analysis of the efficacy for the ITT population, and note that both treatments resulted in a statistically significant difference ($p<0.05$) from placebo. Thus, we believe the study was sufficiently sensitive to discern differences between products. This information is provided on the CD in **Attachment 2.** In addition, a print out of the overall results, including confidence intervals for the primary endpoint (Visit 4), is provided in **Attachment 3.**

6. As requested, we have included the statistical analysis of equivalence for the PP population. Please refer to the CD in **Attachment 2.**

7. The revisions and/or clarifications requested to the list of rules used for assigning missing values for clinical response have been made.

8. All data noted above have been provided on CD in a SAS transport file. These data are accompanied by a description of the content of each file, as well a document file containing a description of each data set and an explanation of the variables included in each SAS data set.

We believe the information contained herein fully responds to the requests presented in the facsimile from Dr. Hixon and as discussed during the conference call on October 24, 2002. Should you have any further questions, please do not hesitate to contact me at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

Vincent Andolina

VA/jbp
Enclosures

APPEARS THIS WAY
ON ORIGINAL

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 8642
FAX: (215) 591 8812

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

Noted: TO Scott F. (Hand to lobeling) 8/28/02 M Andolina

August 23, 2002

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

MINOR AMENDMENT

~~MINOR~~ AMENDMENT
N/Am

FPL

ANDA #65-085
MUPIROCIN OINTMENT USP, 2%
MINOR AMENDMENT- RESPONSE TO AUGUST 1, 2002 REVIEW LETTER

Dear Mr. Buehler:

Teva Pharmaceuticals USA submits herewith a minor amendment to the above-referenced ANDA in response to a review letter received from the Office of Generic Drugs dated August 1, 2002. A copy of this review letter is provided in **Attachment 1** for reference. Please note that comments are addressed in the order presented by the Agency.

1. ——— has responded to their deficiency letter for DMF ——— A copy of the cover letter that accompanied their August 12, 2002 submission is provided in **Attachment 2** for your reference.

2. As requested, we have revised the Total Impurity specification for finished product release to NMT ——, (from NMT ——, and for stability to NMT ——— (from NMT ———. Please note that we also propose to reduce expiration dating from 24-months to 18-months. These limits are based on controlled room temperature data obtained for our ANDA batch as well as on an informal stability study that was conducted on innovator product. Please note that we took steps to obtain innovator samples at or near expiry as suggested in the review letter, however our wholesalers only had available lots that were manufactured recently.

   Please note that this proposal was discussed in an August 13, 2002 conversation between M. Scott Furness, Ph.D., of OGD and Jill Pastore, R.Ph. of Teva Pharmaceuticals USA in which Dr. Furness indicated the above proposal would be found satisfactory by the Agency.

   To ensure that future lots would meet the specifications noted above, we have also tightened the following specifications: ——— (drug substance, finished product release and 18-month stability), ——— (18-month stability) and Total Impurities (drug substance).

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The following tables provide a side by side comparison of the specifications presented in our April 15, 2002 minor amendment versus those proposed herein. Those specifications that have been revised are bolded for ease of review.

***Drug Substance*:**

Related Compound/Impurity	Specification Proposed in April 2002 Amendment	Specification Proposed Herein
[redacted]	NMT [redacted]	**NMT [redacted]**
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
RRT= [redacted]	NMT [redacted]	NMT [redacted]
Any Unidentified Impurity	NMT [redacted]	NMT [redacted]
Total Unidentified Impurities	NMT [redacted]	NMT [redacted]
Total Related Compounds/Impurities	NMT [redacted]	**NMT [redacted]**

Finished Product Release:

Finished Product Related Substance	Release Specification Proposed in April 2002 Amendment	Release Specification Proposed Herein
[redacted]	NMT [redacted]	**NMT [redacted]**
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
RRT= [redacted]	NMT [redacted]	NMT [redacted]
Largest Individual Unidentified Impurity	NMT [redacted] %	NMT [redacted] %
Total Unidentified Degradation Products and Impurities	NMT [redacted]	NMT [redacted] %
Total Impurities	NMT [redacted]	**NMT [redacted]**

Finished Product Stability:

Finished Product Related Substance	Stability Specification Proposed in April 2002 Amendment	18-Month Stability Specification Proposed Herein
[redacted]	NMT [redacted]	**NMT [redacted]**
[redacted]	NMT [redacted]	**NMT [redacted]**
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
RRT= [redacted]	NMT [redacted]	NMT [redacted]
Largest Individual Unidentified Impurity	NMT [redacted] %	NMT [redacted] %
Total Unidentified Degradation Products and Impurities	NMT [redacted]	NMT [redacted]
Total Impurities	NMT [redacted] %	**NMT [redacted] %**

A revised Raw Material Procedures Manual containing the updated API specifications proposed above is provided in **Attachment 3**. Please note that the lots of API used to manufacture the pivotal batch (Rx 0984-034) provided in this ANDA comply with these revised specifications.

In **Attachment 4**, please find the revised Finished Product Procedures Manual containing the updated release and stability specifications noted above. Please note that the pivotal batch (Rx 0984-034) meets these revised release and stability specifications.

In **Attachment 5**, please find a revised Finished Product Stability Protocol, also updated in accord with the above proposal.

Labeling Comments:

1. **Carton**: The Information for Patient section as seen in the insert labeling has been added to the carton labeling as suggested. However, the established name does not appear on each panel due to space constraints. The name does appear on panels 1 and 3 as well as the end flap (which is Teva's format for other FDA-approved semi-solid products). Twelve copies of final print carton labels for the 15 gram and 30 gram package sizes are provided in **Attachment 6**.

2. **Insert**: All suggested revisions have been made to the insert labeling with the exception of the inclusion of the NDC numbers in the How Supplied section. Please note it is not our format to include NDC numbers, which instead can be found on the tube labels and carton labels. Please find twelve copies of final print insert labeling in **Attachment 7**.

3. **Tubes**: Please find in **Attachment 8** twelve copies of final print tube labels for the 15 gram and 30 gram tubes. These labels are identical in content to the draft labels provided in our October 25, 2001 minor amendment.

It is our belief that the information provided herein represents a complete response to the comments set forth in the review letter dated August 1, 2002. Should you have any further questions or comments, please feel free to contact me at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

Vincent Andolina

VA/jbp
Enclosures

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 3000
FAX: (215) 591 8600

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

May 3, 2002

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

BIOEQUIVALENCE AMENDMENT

ORIG AMENDMENT

ANDA #65-085
MUPIROCIN OINTMENT USP, 2%
BIOEQUIVALENCE AMENDMENT- RESPONSE TO APRIL 22, 2002 TELEPHONE REQUEST

Dear Mr. Buehler:

We submit herewith a bioequivalence amendment to the above-referenced pending ANDA in response to a telephone request received from Steve Mazzella of the Office of Generic Drugs, Division of Bioequivalence in an April 22, 2002 conversation with Vincent Andolina of TEVA. Specifically, Mr. Mazzella noted that the compact disc provided in TEVA's April 9, 2002 amendment contains files that cannot be used for analyses. He requested data in either text or SAS format accompanied by a decode file. A follow up call was held between TEVA and OGD on April 29, 2002 to clarify Mr. Mazzella's request. Present for that call were Deborah Jaskot, Vincent Andolina and Li Luo of TEVA, and Dr. Lizzie Sanchez and Dr. H. Li of FDA's Division of Bioequivalence.

Please note that our biostatistics group has provided the following based on their understanding of FDA's request as discussed in the April 29, 2002 conference call:

- Summary from the biostatistics group of the information contained on the compact disc (**Attachment 1**).
- Printout of the raw SAS data sets (**Attachment 2**).
- Printout of the format of the SAS data sets (**Attachment 3**).
- Copy of page 112 of the original ANDA which explains the reason for exclusion of patients from the PP cohort (**Attachment 4**).
- Compact disc containing the requested information (**Attachment 5**).

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We believe the information contained herein fully responds to the Agency's April 22, 2002 request as clarified in the April 29, 2002 teleconference call. Should you have any further questions, please do not hesitate to contact me at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

Vincent Andolina

VA/jbp
Enclosures

APPEARS THIS WAY
ON ORIGINAL

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 3000
FAX: (215) 591 8600

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

April 15, 2002

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

MINOR AMENDMENT

ORIG AMENDMENT
N/AM

ANDA #65-085
MUPIROCIN OINTMENT USP, 2%
MINOR AMENDMENT- RESPONSE TO JANUARY 14, 2002 REVIEW LETTER

Dear Mr. Buehler:

Teva Pharmaceuticals USA submits herewith a minor amendment to the above-referenced ANDA in response to a review letter received from the Office of Generic Drugs dated January 14, 2002. A copy of this review letter is provided in **Attachment 1** for reference. Please note that comments are addressed in the order presented by the Agency.

1. Regarding tightening of the finished product stability specifications for [redacted] Total Unidentified Degradation Products/Impurities and Total Impurities, please note that we have reviewed all currently available data as well as data obtained for the original release of the active pharmaceutical ingredient (API) for this product. As a result of these reviews, we have revised several of our API release specifications in order to allow lower impurity stability specifications for the finished product. Therefore, we have also revised our finished product release and stability specifications. Please note that the stability specification for [redacted] was increased based on the increase seen at 24-months for the pivotal batch (Rx 0984-034), as well as for the IND batch (Rx 0984-009) which was submitted in a November 10, 1999 Investigational New Drug Application.

   The following tables provide a side by side comparison of the specifications presented in our October 25, 2001 minor amendment versus those proposed herein for the API and finished product. Those specifications that have been revised are bolded for ease of review.

***Drug Substance*:**

Related Compound/Impurity	Specification Proposed in October 2001 Amendment	Specification Proposed Herein
[redacted]	NMT [redacted]	**NMT** [redacted]
[redacted]	NMT [redacted]	**NMT** [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
RRT= [redacted]	NMT [redacted]	NMT [redacted]
Any Unidentified Impurity	NMT [redacted]	NMT [redacted]
Total Unidentified Impurities	N/A	**NMT** [redacted]
Total Related Compounds/Impurities	NMT [redacted]	NMT [redacted]

Finished Product Release:

Finished Product Related Substance	Release Specification Proposed in October 2001 Amendment	Release Specification Proposed Herein
[redacted]	NMT [redacted]	**NMT** [redacted]
[redacted]	NMT [redacted]	**NMT** [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
RRT= [redacted]	NMT [redacted]	NMT [redacted]
Largest Individual Unidentified Impurity	NMT [redacted] %	NMT [redacted] %
Total Unidentified Degradation Products and Impurities	NMT [redacted]	**NMT** [redacted] %
Total Impurities	NMT [redacted]	**NMT** [redacted] %

Finished Product Stability:

Finished Product Related Substance	Stability Specification Proposed in October 2001 Amendment	Stability Specification Proposed Herein
[redacted]	NMT [redacted]	**NMT** [redacted] %
[redacted]	NMT [redacted]	**NMT** [redacted] %
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
RRT= [redacted]	NMT [redacted]	NMT [redacted]
Largest Individual Unidentified Impurity	NMT [redacted] %	NMT [redacted] %
Total Unidentified Degradation Products and Impurities	NMT [redacted] %	**NMT** [redacted] %
Total Impurities	NMT [redacted] %	NMT [redacted] %

A revised Raw Material Procedures Manual containing the updated API specifications proposed above is provided in **Attachment 2**. Please note that the lots of API used to manufacture the pivotal batch (Rx 0984-034) provided in this ANDA comply with these revised specifications.

In **Attachment 3**, please find the revised Finished Product Procedures Manual containing the updated release and stability specifications noted above. Please note that the pivotal batch (Rx 0984-034) meets these revised release and stability specifications.

In **Attachment 4**, please find a revised Finished Product Stability Protocol, also updated in accord with the above proposal. Updated stability reports for the pivotal batch Rx 0984-034 (long-term controlled room temperature as well as accelerated studies) containing the revised specifications noted herein are provided in **Attachment 5**. In addition, long-term controlled room temperature stability data are provided in **Attachment 5** for the IND batch Rx 0984-009 as discussed in response #1. Please note that the stability reports for the IND batch reflect the specifications that were in place at the time of testing of that batch, and therefore do not reflect the updated specifications proposed herein.

2. Please note that [redacted] has responded to the deficiency letter concerning their DMF [redacted] for [redacted], and a copy of the cover letter that accompanied their March 7, 2002 response is provided in **Attachment 6** for your reference.

In addition, please note that in our minor amendment dated October 25, 2001, we added [redacted] testing as an in-process test. Per a commitment made in that amendment, please find in **Attachment 7** a revised master production batch record which includes instructions for obtaining samples for testing of [redacted]. [redacted] testing will be conducted on all future commercial batches of this product according to the test and specification proposed in the October 25, 2001 amendment.

It is our belief that the information provided herein represents a complete response to the comments set forth in the review letter dated January 14, 2002. Should you have any further questions or comments, please feel free to contact me at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

Vincent Arcolesi

VA/jbp
Enclosures

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 3000
FAX: (215) 591 8600

ANDA #65-085

MUPIROCIN OINTMENT USP, 2%

MINOR AMENDMENT - RESPONSE TO JANUARY 14, 2002 REVIEW LETTER

In accord with the 21 CFR 314.96(b), TEVA Pharmaceuticals USA hereby certifies that the field copy is a true copy of the technical section of this submission and has been provided to the Philadelphia District Office.

Vincent Andolina

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

4/15/2002
Date

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 3000
FAX: (215) 591 8600

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

April 9, 2002

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

BIOEQUIVALENCE AMENDMENT

ORIG AMENDMENT
N/AB

ANDA #65-085
MUPIROCIN OINTMENT USP, 2%
BIOEQUIVALENCE AMENDMENT- RESPONSE TO MARCH 27, 2002 TELEPHONE REQUEST

Dear Mr. Buehler:

We submit herewith a bioequivalence amendment to the above-referenced pending ANDA in response to a telephone request received from Steve Mazzella of the Office of Generic Drugs, Division of Bioequivalence in a March 27, 2002 conversation with Philip Erickson of TEVA. Specifically, regarding the electronic information provided for the clinical study, Mr. Mazzella requested confirmation of the inclusion of data under the entries listed within the index, as the reviewer could not access the following information: 1) Skin infection rating scale and global assessment for each patient visit, 2) Bacteriologic response for each patient per visit, 3) Reasons for subject withdrawal, and 4) Reasons for subjects who were excluded from ITT, ITTM, and PP populations. In addition, the reviewer requested explanations of the variables of each of the SAS data sets and an SAS decode format for each SAS variable in the raw data sets.

In response, please find enclosed the following:

1. In **Attachment 1**, please find a compact disc which contains the information noted above in #1-4. These tables had been provided in the original ANDA in hard copy but were inadvertently omitted electronically, therefore the enclosed CD has been provided to include this information electronically. We apologize for any inconvenience this may have caused.

RECEIVED
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OGD / CDER

Specifically, the CD contains the following listings:

- (FDA) D: \SAS612.70\MUPIROCIN\OUTPUT\LISTINGS_LBATCH.LIST

- SAS LOG FILE FOR PROGRAM WHICH CREATED THE OUTPUT LISTINGS: (FDA) D: \SAS612.70\MUPIROCIN\OUTPUT\LISTINGS_LBATCH.LOG

- Explanations of the variables of each of the SAS data sets and an SAS decode format for each SAS variable: (FDA) D: \SAS612.70\MUPIROCIN\DEFINE.DOC

2. In **Attachment 2**, please find an explanation of the variables for each of the SAS data sets as well as a SAS decode format for each variable in the raw data sets. Please note this information is also provided on the CD provided in **Attachment 1** as noted above.

We believe the information contained herein fully responds to the requests made by Mr. Mazzella on March 27, 2002. Should you have any further questions, please do not hesitate to contact me at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

Vincent Andolina

VA/jbp
Enclosures

APPEARS THIS WAY
ON ORIGINAL

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 3000
FAX: (215) 591 8600

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

ORIG AMENDMENT
N/A B

BIOAVAILABILITY

January 21, 2002

BIOEQUIVALENCE AMENDMENT

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

CENTER FOR DRUGS
JAN 2 2 2002
EVALUATION AND RESEARCH

ANDA #65-085
MUPIROCIN OINTMENT USP, 2%
BIOEQUIVALENCE AMENDMENT- RESPONSE TO NOVEMBER 16 AND DECEMBER 5, 2001 REVIEW LETTERS

Dear Mr. Buehler:

We submit herewith a bioequivalence amendment to the above-referenced pending ANDA in response to review letters dated November 16, 2001 and December 5, 2001 from the Office of Generic Drugs, Division of Bioequivalence. Copies of the review letters are provided in **Attachment 1** for reference.

In response to the comments in the November 16, 2001 review letter regarding the methods, criteria used to categorize samples and the range of issues considered in defining and categorizing the samples, we would like to provide the following information:

TEVA's placebo-controlled clinical study comparing our generic formulation of Mupirocin Ointment USP, 2% to SmithKline Beecham's Bactroban® Ointment, 2% began on April 28, 2000. Prior to the commencement of the study, all study medication was blinded by [redacted], the company contracted by TEVA to apply a black, opaque shrink wrap material to all tubes in order to conceal the identity of the manufacturer of the product contained therein. At the time of blinding, the shrink wrap was applied in error, such that the crimp ends of the tubes were not covered by the shrink wrap. SmithKline's product is packaged in tubes with a black line which appears vertically on the crimp seal, while TEVA packaged product in tubes whose crimp end had no marks. To resolve this error, a piece of silver, opaque, tamperproof tape was applied to the crimped end of each tube to conceal the entire crimp. Product was then shipped to clinical sites, and the trial commenced.

During the first round of clinical site monitoring visits, it was discovered that some study medication tubes were being returned by patients to the clinical sites with the silver, opaque tamperproof tape not fully adhered to the tubes. Upon discovery of this issue, corrective processes were immediately put in place at both the clinical packager and the investigative sites to repair all remaining medication that was dispensed after July 1, 2000. Further, a "Returned Study Drug Processing Protocol" was promptly developed at TEVA for determination of the potential that any of the involved parties had become unblinded. TEVA then contacted [redacted] to provide a non-biased assessment of the potential for unblinding of study physicians, study staff, and/or patients. [redacted] agreed to follow the "Returned Study Drug Processing Protocol" for TEVA, and provided a report upon completion of their assessment. Please find the protocol in **Attachment 2**, which provides the justification, procedure and definitions for addressing the issue at hand (this protocol was also provided on pages 206-208 of the original ANDA). [redacted] report was provided to the Agency in a September 21, 2001 Telephone Amendment, and is provided in **Attachment 3** for ease of reference.

As a precaution, prior to [redacted] assessment, the study sample size was increased from 300 patients to 350 patients to ensure enrollment of at least 200 patients who had a positive baseline culture, who received at least one dose of study medication, and whose study medication tube blinding was classified as "unlikely" to have been compromised.

Comments provided in the December 5, 2001 review letter are addressed below in the order they were presented.

1. For specific details regarding the procedure used to carry out the independent audit of the tubes with packaging issues, please refer to the "Returned Study Drug Processing Protocol" provided in **Attachment 2.**

2. As requested, the data were reanalyzed to include only those patients enrolled on or after July 1, 2000. These results demonstrate, as did the analyses provided in the original ANDA, that TEVA's Mupirocin Ointment USP, 2% is bioequivalent to SmithKline Beecham's Bactroban® Ointment, 2%. Please find a description and summary of this reanalysis in **Attachment 4**. In addition, all data tables are provided in hard copy as well as on diskette in **Attachment 5**.

We trust that the information provided herein fully responds to the Agency's November 16 and December 5, 2001 review letters. Should you have any further questions or concerns, please feel free to contact me by telephone at (215) 591-8642 or via facsimile at (215) 591-8812.

Sincerely,

Vincent Andolina

VA/jbp
Enclosures

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 3000
FAX: (215) 591 8600

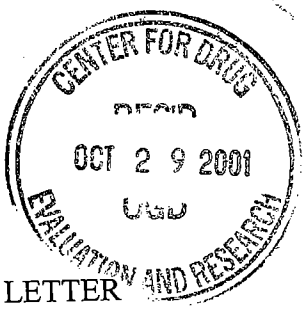
Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

October 25, 2001

ORIG AMENDMENT
N/AM

MINOR AMENDMENT

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773



ANDA #65-085
MUPIROCIN OINTMENT USP, 2%
MINOR AMENDMENT- RESPONSE TO APRIL 26, 2001 REVIEW LETTER

Dear Mr. Buehler:

We submit herewith a minor amendment to the above-referenced pending ANDA for Mupirocin Ointment USP, 2% in response to a review letter received from the Office of Generic Drugs dated April 26, 2001. A copy of the review letter is provided in **Attachment 1** for reference. Responses are provided in the order in which comments were presented in the review letter.

A. Deficiencies

1. In response to your request, we note that the comparison of ANDA and production formulae chart as provided on page 2610 in the original ANDA notes the theoretical amount of ointment produced per the master and executed batch formulae (i.e. [redacted]). However, we have also updated the composition chart originally provided on page 2491 to include the theoretical batch yield. Please find this revised chart as well as page 2610 as originally submitted in the ANDA in **Attachment 2**.

2. Regarding the GC residual solvent test, please note that it is our practice to report Limit of Detection only on limit tests. It is generally accepted that the Limit of Quantitation is [redacted] greater than the Limit of Detection. In our validation report (submitted in the original ANDA on pages 2754- 2775), we listed the detection limits for [redacted] respectively. Consequently, the Limits of Quantitation are [redacted]

respectively. Please note that these figures are significantly lower than the limits set in the specification (respectively).

3. Presently, there are no formally established time limits on production with regard to storage or holding of intermediates during the manufacture of this product. The manufacture and packaging of the ANDA Lot #0984-034 began on January 27, 2000 and was completed on February 4, 2000. Therefore, manufacture and packaging occurred within a period of nine days, which is well within FDA guidelines of completion within thirty days. Please note that it is our standard practice at the time of process validation to establish batch hold times for individual products. Therefore, during process validation for Mupirocin Ointment USP, 2%, the manufacturing process will be assessed to identify the maximum bulk storage time for this product. To accomplish this task,

4. As requested, please note that we have added testing as an in-process control. Please refer to the Finished Product Procedures Manual in **Attachment 3** which has been revised to include this test with the specification "the average of the individual test results is of the labeled amount of Mupirocin, with a relative standard deviation of NMT . The master production batch record for this product will be updated to include instructions for obtaining samples for , testing, and will be submitted to the Agency at the time of the next amendment to this file.

5. Please note that the Minimum Fill test results reported on the drug product Certificate of Analysis correspond to the average net content of ten containers in accord with USP <755>. For clarification purposes, the Finished Product Procedures Manual has been updated to state that the procedure involves averaging the net content of ten containers. Please refer to page 4 of the manual provided in **Attachment 3**.

6. With respect to your request to tighten the release and stability specifications for Related Compounds and Impurities, please note that we were reluctant to tighten finished product impurity specifications due to existing raw material impurity specifications. We contacted the , to see if any of the raw material specifications could be tightened, which in turn would allow us to tighten the finished product specifications. In that process, it was discovered that raw material related substances specifications had been revised in a February 27, 2000 correspondence to FDA related to DMF , and the revisions were inadvertently not communicated to TEVA. As a result, we believe it necessary to

revise our raw material specifications to be in accord with those contained in [redacted] DMF such that we may continue to receive this active ingredient from [redacted]

For ease of review, the following table shows the raw material specifications for related substances as submitted in our original ANDA and those proposed herein which are in accord with specifications contained in [redacted] DMF [redacted] Those specifications that have been revised or added are bolded.

Drug Substance Related Substance	**Specification in Original ANDA**	**Specification Proposed Herein**
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	**NMT** [redacted]
[redacted]	NMT [redacted]	**NMT** [redacted]
[redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	**NMT** [redacted]
RRT = [redacted]	N/A	**NMT** [redacted]
Individual Unidentified Impurity	NMT [redacted]	**NMT** [redacted]
Total Impurities	NMT [redacted]	NMT [redacted]

Please find a revised Raw Material Procedures Manual for Mupirocin USP in **Attachment 4**. In addition, the certificates of analysis for the [redacted] lots of Mupirocin USP used in manufacture of the pivotal batch (#9369 and #9255) have been updated to note the revised specifications and are provided in **Attachment 5**.

Considering the above specifications, we conducted a review of all data available for finished product and have tightened release specifications [redacted] Total Unidentified) and stability specifications [redacted] and Total Unidentified) where appropriate. Please note that the specification for [redacted] was increased to NMT [redacted] and RRT = [redacted] was added, to reflect [redacted] raw material specifications. For ease of review, the following table shows the finished product specifications proposed in the original ANDA and those revised specifications proposed herein. Again, those specifications which have been revised or added are bolded.

Finished Product Related Substance	Specification in Original ANDA (Release and Stability)	Release Specification Proposed Herein	Stability Specification Proposed Herein
[redacted]	NMT [redacted]	**NMT** [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	**NMT** [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	**NMT** [redacted]	**NMT** [redacted]
[redacted]	NMT [redacted]	**NMT** [redacted]	**NMT** [redacted]
[redacted]	NMT [redacted]	NMT [redacted]	NMT [redacted]
[redacted]	NMT [redacted]	**NMT** [redacted]	**NMT** [redacted]
RRT = [redacted]	N/A	**NMT** [redacted]	**NMT** [redacted]
Largest Individual Unidentified Impurity	NMT [redacted]	NMT [redacted]	NMT [redacted]
Total Unidentified Degradation Products and Impurities	NMT [redacted]	**NMT** [redacted]	**NMT** [redacted]
Total Impurities	N/A	**NMT** [redacted]	**NMT** [redacted]

Please refer to the revised Finished Product Procedures Manual in **Attachment 3** and the Finished Product Stability Protocol in **Attachment 6** for these revised specifications. In addition, the finished product certificates of analysis (15 gram and 30 gram tube) have been updated to note the revised specifications and are provided in **Attachment 7**. Please note that they do not reflect the test and specification for [redacted] (proposed herein) as this test was not a requirement at the time of batch release. Certificates of analysis for all future batches will include this data.

7. As requested, a specification for Total Impurities has been added for Related Compounds and Impurities for release and stability (see table above). Please refer to the Finished Product Procedures Manual in **Attachment 3** and the Finished

Product Stability Protocol in **Attachment 6** which contain this additional specification.

8. The stability commitment has been revised as requested and is provided in **Attachment 6**.

9. In accord with Teva's internal procedures, the drug product expiration dating is calculated from the date [redacted]. As can be seen on page one of the commercial batch card provided in the original ANDA (page 2598 of the ANDA), the manufacturing start date begins on the day the active is added to the batch (page 8, step 3 of the batch instructions), and the expiration date is calculated using this date. The commercial batch card from the original ANDA is provided in **Attachment 8** for ease of reference (ANDA pages 2598- 2608).

B. Notes and Acknowledgments

1. As requested, please find updated stability summary reports containing all available long-term stability data in **Attachment 9**. Stability reports for the controlled room temperature studies have been updated to note the revised specifications contained in this amendment and are also provided in this attachment.

2. Please note that [redacted] the holder of DMF # [redacted], responded to the Agency regarding their deficiencies on June 7, 2001. A copy of the cover letter which accompanied their response is provided in **Attachment 10** for your reference.

C. Labeling

1. General: Please note that the storage temperature has been revised as requested throughout the labels and labeling.

2. Container (tube): All requested revisions have been incorporated in the container labels. Please find four copies of draft container labels as well as a comparison document showing the changes between these labels and those last submitted to the Agency in **Attachment 11**.

3. Carton: The requested revision to the storage temperature has been incorporated in the carton labeling. Four draft copies as well as a comparison document showing the changes between this carton and the carton last submitted to the Agency are provided in **Attachment 12**.

4. Insert: All requested revisions have been incorporated in the insert labeling. Four draft copies are provided in **Attachment 13**, along with a comparison document showing the changes between this version and the last version submitted to the Agency.

We look forward to your continued review and approval of ANDA #65-085. Should there be any further questions, please do not hesitate to contact me by phone at (215) 591-8642 or by facsimile at (215) 591-8812.

Sincerely,

Vincent Andolina

VA/jbp
Enclosures

Administrative Offices:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 3000
FAX: (215) 591 8600

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

NEW CORRESP

BW

September 21, 2001

TELEPHONE AMENDMENT-
BIOEQUIVALENCE INFORMATION

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ANDA #65-085
MUPIROCIN OINTMENT USP, 2%
TELEPHONE AMENDMENT- BIOEQUIVALENCE INFORMATION

Dear Mr. Buehler:

We submit herewith an amendment to the above-referenced pending ANDA for Mupirocin Ointment USP, 2% in response to a voice mail message left by Mr. Steve Mazzella of the Office of Generic Drugs for Vincent Andolina of TEVA Pharmaceuticals USA on September 18, 2001. Specifically, Mr. Mazzella requested a copy of a report from [redacted] regarding blinded clinical supplies, which was referenced in the original ANDA.

As requested, please find enclosed the [redacted] report. As described in the clinical study report provided in the original ANDA, [redacted] evaluated the study drug tubes using the Returned Study Drug Processing Protocol which was provided in Appendix B1 (pages 206-208) of the submission. Please note that the [redacted] report contained herein, dated December 14, 2000, reports that 98 tubes were "somewhat likely" to have been compromised. In the ANDA however, it is reported that 109 tubes were "somewhat likely" to have been compromised. The explanation for this discrepancy is that there were eleven (11) tubes that could not be evaluated by [redacted] because they were never returned by patients. These patients either lost their study medication tubes or were lost to follow up. Because these eleven tubes had been dispensed prior to the date that the issue with the tubes was known to exist, TEVA conservatively classified these tubes as "somewhat likely" to have been compromised for a total of 109 tubes in this category rather than the 98 tubes reported by [redacted]
We look forward to your continued review of ANDA #65-085. Should you have any further questions, please do not hesitate to contact me by phone at (215) 591-8642 or by facsimile at (215) 591-8812.

Sincerely,

Vincent Andolina/PE

VA/jbp
Enclosure

ANDA 65-085

TEVA Pharmaceuticals USA
Attention: Vincent Andolina
1090 Horsham Road
P.O. Box 1090
North Wales, PA 19454

FEB 21 2001

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 made to the telephone conversation dated February 9, 2001 and to your correspondence dated February 13, 2001.

NAME OF DRUG: Mupirocin Ointment USP, 2%

DATE OF APPLICATION: January 11, 2001

DATE (RECEIVED) ACCEPTABLE FOR FILING: January 12, 2001

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:

Mark Anderson
Project Manager
(301) 827-5849

Sincerely yours,

Gregory S. Davis for

Wm Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Corporate Headquarters:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 3000
FAX: (215) 591 8600

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

February 13, 2001

NEW CORRESP
NC

NEW CORRESPONDENCE

Gary Buehler, Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ANDA #65-085
MUPIROCIN OINTMENT USP, 2%
NEW CORRESPONDENCE

Dear Mr. Buehler:

We submit herewith new correspondence to the above-referenced ANDA for Mupirocin Ointment USP, 2% in response to a telephone call held between Mr. Paras Patel of the Office of Generic Drugs and Vincent Andolina of TEVA Pharmaceuticals USA on February 9, 2001. Specifically, Mr. Patel requested the complete addresses for the clinical sites noted on page 92 of TEVA's ANDA for this product. As requested, a list containing all clinical site addresses in the order presented on page 92 is provided.

We look forward to your continued review of ANDA #65-085. Should there be any further questions, please do not hesitate to contact me by phone at (215) 591-8642 or by facsimile at (215) 591-8812.

Sincerely,

Vincent Andolina

VA/jbp
Enclosure

Corporate Headquarters:
TEVA PHARMACEUTICALS USA
1090 Horsham Road, PO Box 1090
North Wales, PA 19454-1090

Phone: (215) 591 3000
FAX: (215) 591 8600

Vincent Andolina, RAC
Director, Regulatory Affairs
Liquids, Semisolids and Specialty Projects

labeling review drafted 4/12/01 A. Vezza

505(j)(2)(A) OK 21-FEB 2001

January 11, 2001

Gary Buehler, Acting Director
Office of Generic Drugs
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIGINAL ABBREVIATED NEW DRUG APPLICATION
MUPIROCIN OINTMENT USP, 2%

Dear Mr. Buehler:

We submit herewith an abbreviated new drug application for the drug product Mupirocin Ointment USP, 2%.

Enclosed are archival and review copies assembled in accord with Office of Generic Drugs February 1999 Guidance for Industry: Organization of an ANDA (OGD #1, Rev. 1). These copies are presented in a total of 15 volumes; 7 for the archival copy and 8 for the review copy.

The application contains a full report of a multi-center, double-blind, placebo-controlled, three-way parallel design clinical study which compared Mupirocin Ointment USP, 2%, manufactured by TEVA Pharmaceuticals USA to the reference listed drug, Bactroban® (mupirocin) 2% Ointment manufactured by SmithKline Beecham.

We look forward to your review and comment. Should there be any questions regarding the information contained herein, please do not hesitate to contact me by phone at (215) 591-8642 or by facsimile at (215) 591-8812.

Sincerely,

Vincent Andolina

VA/jbp
Enclosures

CENTER FOR DRUG
RECD
JAN 12 2001
OGD
EVALUATION AND RESEARCH