

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-055

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**
*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

NDA NUMBER

22-055

NAME OF APPLICANT / NDA HOLDER

Glaxo Group Ltd.
d/b/a GlaxoSmithKline

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

ALTABAX

ACTIVE INGREDIENT(S)

Retapamulin

STRENGTH(S)

1%

DOSAGE FORM

Ointment

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

US 6,281,226*

This patent was submitted to the USPTO for Reissue on July 30, 2003. The Reissue application was allowed on June 28, 2005, and the issue fee was paid on September 26, 2005. The Reissue patent has not yet granted.

b. Issue Date of Patent

8/28/2001

c. Expiration Date of Patent

10/27/2018

d. Name of Patent Owner

SmithKline Beecham Plc.

Address (of Patent Owner)

Attn: Vice President, Corporate Intellectual Property

709 Swedeland Road

UW 2220, P.O. Box 1539

City/State

King of Prussia, PA

ZIP Code

19406-0939

FAX Number (if available)

(610) 270-5090

Telephone Number

(610) 270-5021

E-Mail Address (if available)

charles.m.kinzig@gsk.com

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

- 2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No
- 2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No
- 2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No
- 2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.
- 2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No
- 2.6 Does the patent claim only an intermediate? Yes No
- 2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

- 3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No
- 3.2 Does the patent claim only an intermediate? Yes No
- 3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

- 4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No
- 4.2 Patent Claim Number (as listed in the patent) Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No
- 4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

6 Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed
05/15/2006



NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name
James C Kellerman

Address
GlaxoSmithKline
709 Swedeland Road
UW 2220, P.O. Box 1539

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King of Prussia, PA

ZIP Code
19406-0939

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The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

REQUEST FOR MARKETING EXCLUSIVITY

NDA 22-055

Retapamulin 1% Ointment

for the treatment of impetigo.

Under Sections 505(c)(3)(E)(iii) and 505(j)(5)(F)(iii) of the Federal Food, Drug and Cosmetic Act and Section 314.108(b)(4) of Title 21 of the Code of Federal Regulations (CFR), GlaxoSmithKline hereby requests 3 years of exclusivity from the date of approval for retapamulin 1% ointment for the treatment of impetigo.

GlaxoSmithKline is entitled to such exclusivity as this New Drug Application (NDA) contains reports of the following new clinical investigations (other than bioavailability studies) that are essential to the approval of the NDA and that were conducted by GlaxoSmithKline. The investigations are "essential to approval of the application" in that the application could not be approved by the FDA without it them:

TOC100224 A Randomised, Observer-blind, Multi-centre, Non-inferiority, Comparative, Phase III Study of the Safety and Efficacy of Topical 1% SB-275833 Ointment, Applied Twice Daily for 5 Days, versus Topical 2% Sodium Fusidate Ointment Applied Three Times Daily for 7 Days in the Treatment of Adult and Paediatric Subjects with Impetigo, and

TOC103469 A Randomised, Double-blind, Multicentre, Superiority Placebo-controlled, Phase III Study to Assess the Efficacy and Safety of Topical 1% SB-275833 Ointment versus Placebo Ointment Applied Twice Daily for 5 days in the Treatment of Adults and Paediatric Subjects with Impetigo.

To the best of GlaxoSmithKline's knowledge, the above referenced clinical investigations are "new" in that the results have not been relied upon by FDA to demonstrate substantial evidence of effectiveness of a previously approved drug product for any indication or of safety for a new patient population and do not duplicate the results of any such investigations.

EXCLUSIVITY SUMMARY

NDA # 22-055

SUPPL # n/a

HFD # 520

Trade Name Altabax

Generic Name retapamulin ointment, 1%

Applicant Name Glaxo Group Limited d/b/a GlaxoSmithKline

Approval Date, If Known April 12, 2007

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

3 years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

N/A

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)

IF "YES," GO TO PART III

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of

summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1	YES <input type="checkbox"/>	NO <input type="checkbox"/>
Investigation #2	YES <input type="checkbox"/>	NO <input type="checkbox"/>

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1	YES <input type="checkbox"/>	NO <input type="checkbox"/>
Investigation #2	YES <input type="checkbox"/>	NO <input type="checkbox"/>

Investigation #1

YES
Explain:

!
!
! NO
! Explain:

Investigation #2

YES
Explain:

!
!
! NO
! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES NO

If yes, explain:

Name of person completing form: Maureen Dillon-Parker
Title: Chief, Project Management Staff
Date: 3-15-07

Name of Office/Division Director signing form: Edward Cox, MD
Title: Acting Office Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

/s/

Maureen Dillon-Parker
5/2/2007 08:25:47 AM
NDA 22-055/Exclusivity Checklist

Edward Cox
5/2/2007 08:43:17 AM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA # : 22-055 Supplement Type (e.g. SE5): n/a Supplement Number: n/a

Stamp Date: 6-12-06 PDUFA Goal Date: 4-12-07

HFD-520 Trade and generic names/dosage form: Altabax (retapamulin ointment) 1%

Applicant: Glaxo Group Limited d/b/a GlaxoSmithKline Therapeutic Class: topical antibiotic

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? *

- Yes. Please proceed to the next section.
 No. PREA does not apply. Skip to signature block.

* SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.

Indication(s) previously approved (please complete this section for supplements only): none

Each indication covered by current application under review must have pediatric studies: *Completed, Deferred, and/or Waived.*

Number of indications for this application(s): 1

Indication #1: Impetigo

Is this an orphan indication?

- Yes. PREA does not apply. Skip to signature block.
 No. Please proceed to the next question.

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
 No: Please check all that apply: XX Partial Waiver XX Deferred XX Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
 Disease/condition does not exist in children
 Too few children with disease to study
 There are safety concerns
 Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies
--

Age/weight range being partially waived (fill in applicable criteria below):

Min _____ kg _____ mo. 0 yr. _____ Tanner Stage _____
 Max _____ kg _____ mo. 2 yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
 Disease/condition does not exist in children
 Too few children with disease to study
 There are safety concerns
 Adult studies ready for approval
 Formulation needed
 Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):

Min _____ kg _____ mo. 2 yr. _____ Tanner Stage _____
 Max _____ kg _____ mo. 9 yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
 Disease/condition does not exist in children
 Too few children with disease to study
 There are safety concerns
 Adult studies ready for approval
 Formulation needed

Other: A protocol design issue regarding a collection of samples for pharmacokinetic testing; specifically, the number of blood draws in infants need to be resolved. Adult population ready for approval.

Date studies are due (mm/dd/yy): 12/31/08

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min _____ kg _____ mo. 9 yr. _____ Tanner Stage _____
 Max _____ kg _____ mo. _____ yr. <18 Tanner Stage _____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

NDA 22-055

Page 3

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA 22-055
HFD-960/ Rosemary Addy or Grace Carmouze

**FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG
DEVELOPMENT, HFD-960, 301-594-7337.
(revised 6-23-2005)**

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: _____

Is this an orphan indication?

- Yes. PREA does not apply. Skip to signature block.
- No. Please proceed to the next question.

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
- No: Please check all that apply: ___ Partial Waiver ___ Deferred ___ Completed
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below)::

Min _____	kg _____	mo. _____	yr. _____	Tanner Stage _____
Max _____	kg _____	mo. _____	yr. _____	Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is

complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below)::

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA 21-984
HFD-960/ Rosemary Addy or Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

(revised 6-23-2005)

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

/s/

Maureen Dillon-Parker
4/12/2007 07:52:17 PM
NDA 22-055; Pediatric Page

NDA 22-055, Retapamulin Ointment 1%
Treatment for impetigo

DEBARMENT CERTIFICATION

GlaxoSmithKline hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug and Cosmetic Act in connection with this application.



Charles E. Mueller or Mertie V. Snead
Director, North America Clinical Compliance
Worldwide Regulatory Compliance



Date

DAIOP requested that GSK submit, as a major amendment from GSK's study of Altabax vs. placebo for the treatment of impetigo. results

On November 21 2006, DAIOP presented the Altabax application at an internal Regulatory Briefing so that CDER/OND colleagues and management could provide feedback on proposals and approaches for defining non-inferiority margins for indications related to uncomplicated skin infections such as impetigo. Summary comments from the briefing are discussed below in sections of this memo.

By the December 29, 2006 action date for one impetigo study (retapamulin versus placebo) led the clinical reviewers, Dr. Murray, and me to conclude that substantial evidence of

efficacy and safety had been demonstrated for [REDACTED]. Dr. Edward Cox, acting OAP office director, however, did not agree with approval of Altanax for [REDACTED] studies alone and so indicated in an approvable letter of December 22, 2006:

"...We completed our review of this application, as amended, and it is approvable. Before the application may be approved, however, [REDACTED] Altanax (retapamulin ointment) 1% [REDACTED]. This evidence could be provided by the approval of Altanax for a closely related skin infection, such as impetigo. The [REDACTED]

2. CMC

2.1. General Product Quality considerations

According to the Office of New Drug Quality Assessment (ONDQA) review prepared by Drs. Sahmugam, Ocheltree and Matecka, the original application and subsequent amendments contained adequate information supporting the quality of the drug substance and drug product.

2.2. Facilities Review/Inspection

An overall compliance recommendation was made on Aug. 17, 2006 with an acceptable cGMP status for all facilities involved in the manufacture, packaging, and testing of the drug substance and product.

2.3. Issues Needing Resolution

One CMC issue still to be addressed concerns final review of Carton/Container Labels and Foil Sample/12-sample box. Please see CMC reviews by Drs. Mateka and Schmuff. It appears that Dr. Mateka addressed the labeling on the 5g, 10g, and 15g

¹ Koning S, van Suijlekom-Smit LWA, Nouwen JL, Verduin CM, Bernsen RMD, Oranje AP, Thomas S, van der Wouden JC. Fusidic acid cream in the treatment of impetigo in general practice: double blind randomised placebo controlled trial British Medical Journal 2002; 324: 1-5.

3 Page(s) Withheld

2 Trade Secret / Confidential

 Draft Labeling

 Deliberative Process

Withheld Track Number: Administrative-

Phase 3/Essential Clinical Studies- Impetigo

Protocol 103469 was a double-blind, randomized study comparing Altabax to placebo for the treatment of impetigo.

Results from Study 103469 were also included in NDA 22-055. At the time of the December 22, 2006 PDUFA goal date, a full review of NDA 22-055, including routine inspections, was not yet complete.

GSK provided data from two studies (103469 and 100224) to support approval of impetigo. These non-IND studies were conducted outside of the United States. The studies were similar in design, though one compared retapamulin to placebo, while the other compared retapamulin to sodium fusidate (not approved in the US). Study 103469 was a multicenter, randomized, double-blind study comparing retapamulin to placebo (retapamulin or placebo ointment BID for 5 days) in the treatment of impetigo in patients ≥ 9 months old to adults. Study 100224 was a multicenter, randomized, single-blind study comparing retapamulin to sodium fusidate ointment (retapamulin ointment BID for 5 days, sodium fusidate ointment TID for 7 days) in the treatment of impetigo in patients ≥ 9 months old to adults. The studies were randomized two retapamulin ointment patients to one placebo or fusidate ointment patient.

The data for study 103469 show a robust treatment effect for Altabax compared to placebo for the treatment of impetigo. The difference in clinical success was 36-39% (PPC and ITT) with a lower confidence bound of not less than 22%. The treatment effect in this study is highly consistent with that of other drugs evaluated in placebo controlled studies.

Sodium fusidate ointment is not approved in the US. The results of the Altabax versus sodium fusidate study, nevertheless, are noteworthy. Analyses show the point estimates for clinical and bacteriological efficacy of retapamulin ointment to be 2% to 6% higher than those of sodium fusidate and statistically superior in three of four population analyses at the end of therapy. This is additional supportive evidence of the antibacterial effectiveness of retapamulin ointment.

Results of these studies appear in the four tables below.

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Study 103469: Clinical Response at End of Therapy & at Follow-up by Population

	Retapamulin		Placebo		Difference in Success Rates (%)	95 % CI (%)
	n/N	Success Rate (%)	n/N	Success Rate (%)		
End of Therapy						
PPC	111/124	89.5	33/62	53.2	36.3	(22.8, 49.8)
ITTC	119/139	85.6	37/71	52.1	33.5	(20.5, 46.5)
PPB	96/107	89.7	26/52	50.0	39.7	(25.0, 54.5)
ITTB	101/114	88.6	28/57	49.1	39.5	(25.2, 53.7)
Follow Up						
PPC	98/119	82.4	25/58	43.1	39.2	(24.8, 53.7)
ITTC	105/139	75.5	28/71	39.4	36.1	(22.7, 49.5)
PPB	86/102	84.3	18/48	37.5	46.8	(31.4, 62.2)
ITTB	91/114	79.8	19/57	33.3	46.5	(32.2, 60.8)

n = number with clinical success outcome, N = number in analysis population, PPC = Clinical Per Protocol Population, ITTC = Clinical Intent to Treat Population, PPB = Bacteriological Per Protocol Population, ITTB = Bacteriological Intent to Treat

Study 103469: Clinical Response by Baseline Pathogen in Clinical ITT Population (ITTC)

Pathogen	Retapamulin		Placebo	
	n/N	Success Rate (%)	n/N	Success Rate (%)
End of Therapy				
<i>Staphylococcus aureus</i> (Methicillin-susceptible)	84/95	88.4	27/51	52.9
<i>Streptococcus pyogenes</i>	30/34	88.2	3/8	37.5
Follow Up				
<i>Staphylococcus aureus</i> (Methicillin-susceptible)	75/95	78.9	18/51	35.3
<i>Streptococcus pyogenes</i>	29/34	85.3	1/8	12.5

n = number with clinical success outcome, N = number in analysis population

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Study 100224: Clinical Response at End of Therapy & at Follow-up by Population

	Retapamulin		Sodium Fusidate		Difference in Success Rates (%)	95 % CI (%)
	n/N	Success Rate (%)	n/N	Success Rate (%)		
End of Therapy						
PPC	314/317	99.1	141/150	94.0	5.1	(1.1, 9.0)
ITTC	327/345	94.8	155/172	90.1	4.7	(-0.4, 9.7)
PPB	240/242	99.2	106/114	93.0	6.2	(0.5, 12.6)
ITTB	250/263	95.1	116/131	88.5	6.5	(1.4, 11.0)
Follow Up						
PPC	297/308	96.4	134/143	93.7	2.7	(-1.8, 7.2)
ITTC	310/345	89.9	150/172	87.2	2.6	(-3.3, 8.6)
PPB	227/235	96.6	99/107	92.5	4.1	(-1.4, 9.6)
ITTB	237/263	90.1	111.131	84.7	5.4	(-1.8, 12.5)

n = number with clinical success outcome, N = number in analysis population, PPC = Clinical Per Protocol Population, ITTC = Clinical Intent to Treat Population, PPB = Bacteriological Per Protocol Population, ITTB = Bacteriological Intent to Treat Population

Table 5. Clinical Response at End of Therapy and Follow-Up for Patients With *Staphylococcus aureus* and *Streptococcus pyogenes* at Baseline in the Clinical Per Protocol Population (PPC) – Study TOC 100224

Pathogen	Retapamulin		Sodium Fusidate	
	n/N	Success Rate (%)	n/N	Success Rate (%)
End of Therapy				
<i>Staphylococcus aureus</i>	209/211	99.1	90/97	92.8
Methicillin-susceptible	201/203	99.0	88/95	92.6
Methicillin-resistant	8/8	100	2/2	100
<i>Streptococcus pyogenes</i>	90/92	97.8	32/36	88.9
Follow Up				
<i>Staphylococcus aureus</i>	199/206	96.6	83/90	93.3
Methicillin-susceptible	191/198	96.5	81/88	92.0
Methicillin-resistant	8/8	100	2/2	100
<i>Streptococcus pyogenes</i>	87/91	95.6	31/36	86.1

n = number with clinical success outcome, N = number in analysis population

6.1.1. Issues needing resolution

For the impetigo indications, there are no issues remaining to be resolved.
For the SID indication, as previously discussed, a new study needs to be conducted.

6.2. Safety

The Division has not identified any significant safety issues with Altabax 1% ointment in a safety data base of over 1600 patients receiving Altabax at the recommended dosage and administration. The product is associated with application site irritation, but significant irritation occurred in less than 2% of phase 3 study participants. Notably, and as expected for a topical product, adverse reactions such as diarrhea and gastrointestinal complaints were less than that for the phase 3 study comparator, cephalexin. In addition, although not directly studied, this topical antibiotic would be expect to have less deleterious effects on normal gastrointestinal flora than an oral antibiotic.

7. Risk Minimization Plan

Given the safety profile for the product, no risk minimization plan is recommended at this time.

8. Summary of Regulatory Issues

There are no regulatory issues, including those related to patents or exclusivity that preclude approval of the application.

9. Foreign Regulatory Actions/Status

10. Advisory Committee Meeting

This NDA/product was not taken to an Advisory Committee

11. Proprietary Name/Carton and Container Labels

Names and labels are acceptable.

12. DSI Audits

DSI summarized their findings as follows:

For NDA 20-055, DSI inspected a site in Bangalore, India, and concluded compliance with protocol specified requirements and that the data in support of efficacy and safety are acceptable.

13. Discussion of primary reviewer's comments and conclusions

Mr. David Bostwick performed the primary clinical review of these applications. In his reviews he recommends approval of Altabax ointment for the treatment of impetigo ~~_____~~ due to methicillin susceptible *Staphylococcus aureus* and/or *Streptococcus pyogenes*. I ~~_____~~

~~_____~~ For impetigo, he concludes that Altabax has been established as effective for impetigo up to 100 cm² in total area (up to 10 lesions) caused by *S. aureus* and/or *S. pyogenes*, supported by study 103409 (Altabax versus placebo). The second pivotal study of impetigo was a comparison of Altabax and sodium fusidate ointment. Since sodium fusidate ointment is not approved in the U.S., the reviewer regarded it as a placebo and Altabax would have to be proven superior to it in order for the study to be successful. By the Applicant's analysis, the two products are not statistically dissimilar at follow-up, which is the reviewer's chosen primary efficacy parameter. Therefore, the study was not acceptable as a pivotal clinical study. It was acceptable as a well-performed supportive study.

14. Discussion of secondary reviewer's comments and conclusions

Dr. Jean Mulinde was the team leader for the clinical review of these applications. Dr. Mulinde concurred with the primary reviewer for the ~~_____~~ impetigo indications, concluding the applicant provided substantial evidence of efficacy and safety for Altabax ointment to warrant approval.

~~_____~~
~~_____~~
~~_____~~

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 Deliberative Process

Withheld Track Number: Administrative-

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P U B L I C H E A L T H S E R V I C E
F O O D A N D D R U G
A D M I N I S T R A T I O N
C E N T E R F O R D R U G E V A L U A T I O N A N D
R E S E A R C H

CLINICAL INSPECTION SUMMARY

DATE: 3/21/07

TO: Maureen Dillon-Parker, Regulatory Project Manager
David Bostwick, M.D., Clinical Reviewer
Division of Anti-Infective and Ophthalmology Products, HFD-520

THROUGH: Leslie K. Ball, M.D.
Branch Chief
Good Clinical Practice Branch 2, HFD-47
Division of Scientific Investigations

FROM: Tejashri Purohit-Sheth, M.D.
Clinical Reviewer, GCP 2, HFD-47
Division of Scientific Investigations

SUBJECT: Evaluation of Clinical Inspections

NDA: 22-055

NME: YES

APPLICANT: GlaxoSmithKline

DRUG: Retapamulin 1% Topical Ointment

THERAPEUTIC CLASSIFICATION: Standard Review

INDICATION: Impetigo

CONSULTATION REQUEST DATE: 9/8//2006

DIVISION ACTION GOAL DATE: 3/30/07

PDUFA DATE: 4/12/07

I. BACKGROUND:

GlaxoSmithKline submitted this New Drug Application (sNDA) in support of the efficacy and safety of topical retapamulin 1% ointment in patients with impetigo. The sponsor conducted the following pivotal study in support of this indication: Study # TOC103469, *A Randomized, Double-blind, Multicenter, Superiority Placebo-controlled, Phase III Study to Assess the Efficacy and Safety of Topical 1% SB-275833 Ointment versus Placebo Ointment Applied Twice Daily for 5 days in the Treatment of Adults and Pediatric Subjects with Impetigo.*

A DSI inspection was requested because only foreign data from 17 centers in four countries (Netherlands, India, Peru, and Mexico) were submitted to support this application of a new molecular entity, which was not conducted under IND. Dr. Sumathy's and Dr. Barba-Gomez' site were selected because of relatively higher enrollment.

II. INSPECTION RESULTS (by protocol/site):

Table of Inspected Sites and Inspection Classifications

Name of CI and site #	City, State	Country	Protocol #	Insp. Date	EIR Received Date	Final Classification
Dr. TK Sumathy Site#: 011867	Bangalore, Karnataka	INDIA	TOC103469	1/8-1/11/07	2/13/07	NAI
Dr. Jose Barba-Gomez Site#: 011042	Zapopan, Jalisco	MEXICO	TOC103469	1/8-1/12/07	3/6/07	VAI

Key to Classifications

NAI = No deviation from regulations. Data acceptable.

VAI-No Response Requested= Deviations(s) from regulations. Data acceptable.

VAI-Response Requested = Deviation(s) form regulations. See specific comments below for data acceptability

OAI = Significant deviations for regulations. Data unreliable.

1. Dr. TK Sumathy (Site 011867)

M S Ramaiah Medical College and Hospital
M S R Nagar, M S R IT Post
Bangalore 560 054, Karnataka

a. What was inspected?

This inspection was conducted in accordance with Compliance Program 7348.811 between 1/8-1/11-06. A total of 50 subjects were randomized at this site. The inspection confirmed that informed consent was appropriately obtained in 100% of

subjects and included review of source documents and hard copy reporting for 100% of subjects. All study subject files were reviewed for verification of: 1) entry criteria 2) diagnosis of target disease (impetigo) 3) primary and key secondary efficacy endpoints 4) adequate adverse experience reporting and 5) adequate documentation of concomitant medications.

b. Limitations of inspection

None.

c. General observations/commentary

In general, the investigator was noted to be compliant with federal regulations and the source documents appeared to be complete and well maintained. No significant deviations with respect to any of the key inspectional areas were identified. The Investigator's correspondence files with the IRB, sponsor, and monitor, and drug accountability records were reviewed and found to be acceptable.

No FDA Form 483 was issued to this investigator; however, the Field Inspector discussed two issues with Dr. Sumathy at the end of the inspection. These issues are summarized below:

1. Several study subjects were under the age of 18 at the time of enrollment and the consent documents were signed by the warden or administrator of the residential boarding school. The Field Inspector advised the investigator of the FDA requirement that the IRB appoint an advocate for such wards, who is not affiliated with the institution. Under Indian law, the school warden or administrator is deemed to be a legal guardian.
2. There were recurrent problems with sample transportation between the site and the central laboratory due to severe weather, primarily resulting in degradation of blood samples, for at least one of the study visits for 18 subjects. There were no issues with blood chemistry analyses; however, hematological analyses of the subjects were unable to be completed. A letter from GSK, Signal Evaluation and Risk Management acknowledged this finding and stated that "although the lack of full (i.e. hematological) analysis of these samples was regrettable, GSK does not believe that the safety of these specific subjects was compromised, nor does the absence of hematological analysis for these subjects compromise the overall conclusions of safety analysis of the data generated from in excess of 2000 subjects or the safety analysis of Study TOC103469."

d. Assessment of data integrity:

In general, Dr. Sumathy complied with protocol specified requirements and the data in support of efficacy and safety is deemed acceptable; however, the Review Division will need to evaluate the clinical impact of not having hematologic samples from 18 patients at this site, taking into account the total patient experience with retapamulin.

2. **Dr. Jose Fernando Barba-Gomez: Site #011402**

Instituto Dermatológico de Jalisco
Av. Federalismo
Col. Atemajac del Valle
Zapopan 45190, Jalisco, Mexico

a. What was inspected?

This inspection was conducted in accordance with Compliance Program 7348.811 between 1/8-1/12-06. A total of 25 subjects were randomized at this site. Note that a translator was necessary to evaluate both the records and to interview Dr. Barba-Gomez and his staff. The inspection confirmed that informed consent was appropriately obtained in 100% of subjects and included review of source documents and hard copy reporting for 100% of subjects. All study subject files were reviewed for verification of 1) entry criteria 2) primary and key secondary efficacy endpoints 3) adequate adverse experience reporting 4) adequate documentation of concomitant medications and 5) diagnosis of impetigo.

b. Limitations of inspection

A translator was necessary for verbal communication and review of records. Although Dr. Barba-Gomez appeared to be able to read and write English somewhat, he didn't feel comfortable having conversations in English.

c. General observations/commentary

Study records were maintained on site and appeared well organized and complete for the most part. A randomization list was maintained with the study records, and no deviations were observed. Adverse events and Skin Infection Rating Scores were verified and no significant deviations were observed. The electronic CRFs (e-CRFs) were reviewed and significant differences between the e-CRFs and source documents were not observed.

Although no significant deviations were noted with respect to data verification of the primary efficacy endpoint and adverse event reporting, there were some deviations noted for which an FDA Form 483 was issued, mainly failure to prepare or maintain adequate case histories with respect to observations and data pertinent to the investigation [21 CFR 312.62 (b)]. The findings with respect to this violation are summarized below.

- a. The Gram stain site source data lacked clear identification of person(s) performing the evaluation and dates that the gram stains were done.
- b. Central Laboratory requisition forms, site source records used to document collection and shipment of lesion specimens, were inconsistently and/or inaccurately dated for the date of collection. Examples follow:

- i. For Subject #428, Skin Swab Requisition No. 761745 and Nasal Swab Requisition No. 748926 (erroneously recorded as 748962 on the FDA Form 483) were dated 11/3/05 then changed to 10/21/05.
- ii. For Subject #429, Nasal Swab Requisition No. 418430 was dated 11/18/05 then changed to 12/01/05. Nasal Swab Requisition No. 418430 was dated 12/01/05 then changed to 11/18/05.

***Reviewer Comments:** The examples of inaccurate recordkeeping above are supported by the exhibits provided. With respect to inadequate documentation of Gram stains, there is no identification on pertinent pages as to who completed the evaluations. Note that Jorge Mayorga was the Clinical Director of the In-House Laboratory and was solely responsible for specimen collection (swabs), Gram Stain observations and records, isolate culture and shipment to local and central laboratories for evaluation. Although he was the only individual who did the procedures, and maybe the need to identify himself as the one conducting the evaluation may not have been evident, this does point to inaccurate recordkeeping. Since he was the only individual performing the procedures, it is unlikely that this finding would have any effect on the outcome of the study from a safety or efficacy standpoint.*

The errors and corrections in Central Laboratory Requisition Forms resulted from Dr. Mayorga failing to document the collection date of the specimens; instead he documented when samples were returned from the local laboratory that did microbiological analyses on the nasal and skin swabs. GSK monitors identified the discrepancies and instituted procedures for corrections, leading to the differences in the requisition forms. The FDA Field Inspector was able to verify that the corrected forms represented accurate collection dates. Therefore, these recordkeeping errors are unlikely to affect the outcome of the study with respect to safety and efficacy.

d. Assessment of data integrity:

Although there are several record keeping errors, it is unlikely that these errors will have any impact on the final outcome of study result interpretation, nor does it appear that the rights, safety and welfare of any of the subjects was compromised due to these inaccuracies.

In general, the study appears to have been conducted adequately, and the data generated by this site may be used in support of the respective indication.

III. OVERALL ASSESSMENT OF FINDINGS AND GENERAL RECOMMENDATIONS

In general, the sites adhered to the applicable regulations and good clinical practices governing the conduct of clinical investigations. The inspection of documents supports

that audited subjects existed, met eligibility criteria, received assigned study medication, adhered to protocol and signed informed consent. Although, the inspections documented minor regulatory violations with respect to recordkeeping, there were no significant discrepancies noted with the data listings and source documents at either site.

In general, the study appears to have been conducted adequately, and the data generated by the sites may be used in support of the respective indication, with the following caveats. For Dr. Sumathy's site, the Division will need to evaluate the lack of hematologic analyses of samples from 18 subjects, taking into account the total safety experience thus far with retapamulin.

Follow-Up Actions: None

{See appended electronic signature page}

Tejashri Purohit-Sheth, M.D.
Medical Officer
Good Clinical Branch II
Division of Scientific Investigations

CONCURRENCE:

Supervisory comments

{See appended electronic signature page}

Leslie K. Ball, M.D.
Branch Chief
Good Clinical Practice Branch II
Division of Scientific Investigations

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/s/

Tejashri Purohit-Sheth
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MEDICAL OFFICER

Leslie Ball
3/30/2007 07:18:40 PM
MEDICAL OFFICER

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CC: Archival IND, 1/22-055
HFD-520/Division File
HFD-520/RPM
HFD-520/Reviewers and Team Leaders

NAME AND PHONE NUMBER OF REQUESTER
Maureen Dillon-Parker/#301-796-0706

METHOD OF DELIVERY (Check one)
 DFS ONLY MAIL HAND

SIGNATURE OF RECEIVER

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Maureen Dillon-Parker

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NDA 22-055; Tradename Re-Review Consult



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-055

Glaxo Group Limited d/b/a GlaxoSmithKline
Attention: Debra Hackett
Director, U.S. Regulatory Affairs
One Franklin Plaza
P.O. Box 7929
Philadelphia, PA 19101-7929

Dear Ms. Hackett:

Please refer to your June 12, 2006, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Retapamulin (SB-275833) Ointment, 1%.

We also refer to your submissions dated July 27, and August 10, 2006.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application was filed under section 505(b) of the Act on August 11, 2006, in accordance with 21 CFR 314.101(a).

If you have any questions, call Maureen Dillon-Parker, Regulatory Project Manager, at (301) 796-0706.

Sincerely,

{See appended electronic signature page}

Frances V. LeSane
Chief, Project Management Staff
Division of Anti-Infective and
Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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Frances LeSane
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-055

NDA ACKNOWLEDGMENT

Glaxo Group Limited d/b/a GlaxoSmithKline
Attention: Debra Hackett
Director, US Regulatory Affairs
One Franklin Plaza
P.O. Box 7929
Philadelphia, PA 19101-7929

Dear Ms. Hackett:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Retapamulin Ointment 1% (SB-275833)

Review Priority Classification: Standard (S)

Date of Application: June 12, 2006

Date of Receipt: June 12, 2006

Our Reference Number: NDA 22-055

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on August 11, 2006 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be April 12, 2007.

Under 21 CFR 314.102(c), you may request a meeting with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the ultimate approvability of the application. Alternatively, you may choose to receive a report by telephone.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have submitted pediatric studies with this application. Once the review of this application is complete we will notify you whether you have fulfilled the pediatric study requirement for this application.

Please cite the NDA number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Anti-Infective and Ophthalmology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, call Maureen Dillon-Parker, Regulatory Project Manager, at (301) 796-0706.

Sincerely,

{See appended electronic signature page}

Frances V. LeSane
Chief, Project Management Staff
Division of Anti-Infective and
Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

Frances LeSane
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NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 22-055 Supplement # n/a Efficacy Supplement Type SE- n/a

Proprietary Name: Altabax 1% Ointment
Established Name: retapamulin
Strengths: 1%

Applicant: Glaxo Group Limited d/b/a GlaxoSmithKline
Agent for Applicant (if applicable):

Date of Application: June 12, 2006
Date of Receipt: June 12, 2006
Date clock started after UN: n/a
Date of Filing Meeting: August 3, 2006
Filing Date: August 11, 2006
Action Goal Date (optional): April 12, 2006 User Fee Goal Date: April 12, 2006

Indication(s) requested: Treatment of primary impetigo

Type of Original NDA: (b)(1) (b)(2)
AND (if applicable)
Type of Supplement: (b)(1) (b)(2)

NOTE:

(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application or efficacy supplement is a (b)(2), complete Appendix B.

Review Classification: S P
Resubmission after withdrawal? Resubmission after refuse to file?
Chemical Classification: (1,2,3 etc.) 1
Other (orphan, OTC, etc.) n/a

Form 3397 (User Fee Cover Sheet) submitted: YES NO

User Fee Status: Paid Exempt (orphan, government)
Waived (e.g., small business, public health)

NOTE: If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required by contacting the User Fee staff in the Office of Regulatory Policy. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the product described in the application. Highlight the differences between the proposed and approved labeling. If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the User Fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in any approved (b)(1) or (b)(2) application? YES NO
If yes, explain:

Note: If the drug under review is a 505(b)(2), this issue will be addressed in detail in appendix B.

- Does another drug have orphan drug exclusivity for the same indication? YES NO
- If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES NO

If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- Is the application affected by the Application Integrity Policy (AIP)? YES NO
If yes, explain:
- If yes, has OC/DMPQ been notified of the submission? YES NO
- Does the submission contain an accurate comprehensive index? YES NO
If no, explain:
- Was form 356h included with an authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. agent must sign.
- Submission complete as required under 21 CFR 314.50? YES NO
If no, explain:
- Answer 1, 2, or 3 below (do not include electronic content of labeling as an partial electronic submission).

1. This application is a paper NDA YES
2. This application is an eNDA or combined paper + eNDA YES
This application is: All electronic Combined paper + eNDA
This application is in: NDA format CTD format
Combined NDA and CTD formats

Does the eNDA, follow the guidance?
(<http://www.fda.gov/cder/guidance/2353fnl.pdf>) YES NO

If an eNDA, all forms and certifications must be in paper and require a signature.

If combined paper + eNDA, which parts of the application were submitted in electronic format?

Additional comments:

3. This application is an eCTD NDA. (HYBRID) YES
If an eCTD NDA, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments: This is an electronic NDA in CTD Format

- Patent information submitted on form FDA 3542a? YES X NO
- Exclusivity requested? YES X 3 Years NO
NOTE: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.
- Correctly worded Debarment Certification included with authorized signature? YES X NO
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.
NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as "To the best of my knowledge"
- Are the required pediatric assessment studies and/or deferral/partial waiver/full waiver of pediatric studies (or request for deferral/partial waiver/full waiver of pediatric studies) included? YES X NO
- If the submission contains a request for deferral, partial waiver, or full waiver of studies, does the application contain the certification required under FD&C Act sections 505B(a)(3)(B) and (4)(A) and (B)? YES NO X
- Is this submission a partial or complete response to a pediatric Written Request? YES NO X
If yes, contact PMHT in the OND-IO
- Financial Disclosure forms included with authorized signature? YES X NO
(Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an agent.)
NOTE: Financial disclosure is required for bioequivalence studies that are the basis for approval.
- Field Copy Certification (that it is a true copy of the CMC technical section) YES X NO
- PDUFA and Action Goal dates correct in tracking system? YES X NO
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.
- List referenced IND numbers:
- Are the trade, established/proper, and applicant names correct in COMIS? YES X NO
If no, have the Document Room make the corrections.
- End-of-Phase 2 Meeting(s)? Date(s) n/a NO
If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date(s) May 8, 2006 NO
If yes, distribute minutes before filing meeting.

- Any SPA agreements? Date(s) March 15, 2006 NO
If yes, distribute letter and/or relevant minutes before filing meeting.

Project Management

- If Rx, was electronic Content of Labeling submitted in SPL format? YES X NO
If no, request in 74-day letter.
- If Rx, for all new NDAs/efficacy supplements submitted on or after 6/30/06:
Was the PI submitted in PLR format? YES X NO

If no, explain. Was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request:
- If Rx, all labeling (PI, PPI, MedGuide, carton and immediate container labels) has been consulted to DDMAC? YES NO X
- If Rx, trade name (and all labeling) consulted to OSE/DMETS? YES NO X
- If Rx, MedGuide and/or PPI (plus PI) consulted to ODE/DSRCS?
N/A X YES NO
- Risk Management Plan consulted to OSE/IO? N/A X YES NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling submitted? N/A X YES NO

If Rx-to-OTC Switch or OTC application: N/A

- Proprietary name, all OTC labeling/packaging, and current approved PI consulted to OSE/DMETS? YES NO
- If the application was received by a clinical review division, has DNPCE been notified of the OTC switch application? Or, if received by DNPCE, has the clinical review division been notified? YES NO

Clinical N/A

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? YES NO

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES X NO
If no, did applicant submit a complete environmental assessment? YES NO
If EA submitted, consulted to EA officer, OPS? YES NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES X NO
- If a parenteral product, consulted to Microbiology Team? YES NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: August 3, 2006

NDA #: 22-055

DRUG NAME: Altabax (retapamulin) 1% Ointment

APPLICANT: GlaxoSmithKline

BACKGROUND: Retapamulin is a semi-synthetic derivative of pleuromutilin, isolated through fermentation from *Clitophilus passeckerianus*. This application provides for the first of the pleuromutilin class of antibacterial agents developed specifically for use in humans.

This is a 1% topical ointment being developed to treat impetigo. It is not marketed in any foreign countries and is not being developed in other review Divisions.

ATTENDEES: Janice Soreth, David Bostwick, Jean Mulinde, Terry Peters, Maryam Rafie-Kolpin, Avery Goodwin, Harold Silver for Fred Marsik, Dorota Matecka, Yan Wang, Thamban Valappil, Charles Bonapace, Arzu Selen, Maureen Dillon-Parker

ASSIGNED REVIEWERS (including those not present at filing meeting) :

<u>Discipline/Organization</u>	<u>Reviewer</u>
Medical:	David Bostwick
Secondary Medical:	n/a
Statistical:	Yan Wang
Pharmacology:	Maryam Rafie-Kolpin
Statistical Pharmacology:	n/a
Chemistry:	Dorota Matecka
Environmental Assessment (if needed):	n/a
Biopharmaceutical:	Chuck Bonapace
Microbiology, sterility:	n/a
Microbiology, clinical (for antimicrobial products only):	Avery Goodwin
DSI:	Mathew Thomas
Regulatory Project Management:	Maureen Dillon-Parker
Other Consults:	n/a

Per reviewers, are all parts in English or English translation? YES X NO
If no, explain:

CLINICAL FILE X REFUSE TO FILE

- Clinical site audit(s) needed? YES X NO
If no, explain:
- Advisory Committee Meeting needed? YES, date if known _____ NO X

- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

	N/A	<input type="checkbox"/>	X	YES	<input type="checkbox"/>	NO	<input type="checkbox"/>
CLINICAL MICROBIOLOGY	N/A	<input type="checkbox"/>	FILE X	REFUSE TO FILE	<input type="checkbox"/>		
STATISTICS	N/A	<input type="checkbox"/>	FILE X	REFUSE TO FILE	<input type="checkbox"/>		
BIOPHARMACEUTICS			FILE X	REFUSE TO FILE	<input type="checkbox"/>		
				YES	<input type="checkbox"/>	NO	X
• Biopharm. study site audits(s) needed?							
PHARMACOLOGY/TOX	N/A	<input type="checkbox"/>	FILE X	REFUSE TO FILE	<input type="checkbox"/>		
				YES	<input type="checkbox"/>	NO	X
• GLP audit needed?							
CHEMISTRY			FILE X	REFUSE TO FILE	<input type="checkbox"/>		
				YES	X	NO	<input type="checkbox"/>
• Establishment(s) ready for inspection?				YES	<input type="checkbox"/>	NO	X
• Sterile product?							
If yes, was microbiology consulted for validation of sterilization?				YES	<input type="checkbox"/>	NO	<input type="checkbox"/>

ELECTRONIC SUBMISSION:

Any comments: eCTD

REGULATORY CONCLUSIONS/DEFICIENCIES:

(Refer to 21 CFR 314.101(d) for filing requirements.)

- The application is unsuitable for filing. Explain why:
- The application, on its face, appears to be well-organized and indexed. The application appears to be suitable for filing.
- X No filing issues have been identified.
- Filing issues to be communicated by Day 74. List (optional):

ACTION ITEMS:

1. ✓ Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into COMIS.
2. n/a If RTF, notify everybody who already received a consult request of RTF action. Cancel the EER.
3. n/a If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
4. If filed, complete the Pediatric Page at this time. (If paper version, enter into DFS.)
5. ✓ Convey document filing issues/no filing issues to applicant by Day 74.

Maureen Dillon-Parker
Regulatory Project Manager

THIS APPLICATION IS NOT A 505(b)(2)

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

/s/

Maureen Dillon-Parker
12/7/2006 03:50:50 PM
CSO
NDA 22-055 - Regulatory Filing Review

45 DAY MEETING CHECKLIST

FILEABILITY:

On initial overview of the NDA application:

YES

NO

CLINICAL:

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

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

/s/

Maureen Dillon-Parker
11/15/2006 02:42:12 PM
CSO
NDA 22-055 Clinical Filing Checklist - For archiving

David Bostwick
11/15/2006 02:47:40 PM
MEDICAL OFFICER

Jean Mulinde
11/16/2006 01:34:28 PM
MEDICAL OFFICER

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information

NDA 22-055	Efficacy Supplement Type SE-N/A	Supplement Number N/A
Drug: Altabax (retapamulin ointment) 1%		Applicant: Glaxo Group Limited d/b/a GlaxoSmithKline
RPM: Maureen Dillon-Parker		HFD-520/DAIOP Phone #6-0706
<p>Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) (This can be determined by consulting page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p> <p>If this is a 505(b)(2) application, please review and confirm the information previously provided in Appendix B to the NDA Regulatory Filing Review. Please update any information (including patent certification information) that is no longer correct.</p> <p><input type="checkbox"/> Confirmed and/or corrected</p>		Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)):
❖ Application Classifications:		
<ul style="list-style-type: none"> • Review priority • Chem class (NDAs only) • Other (e.g., orphan, OTC) 		<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority 1
User Fee Goal Dates		April 12, 2007
❖ Special programs (indicate all that apply)		
		<input checked="" type="checkbox"/> None Subpart H <input type="checkbox"/> 21 CFR 314.510 (accelerated approval) <input type="checkbox"/> 21 CFR 314.520 (restricted distribution) <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2
❖ User Fee Information		
<ul style="list-style-type: none"> • User Fee • User Fee waiver • User Fee exception 		<input checked="" type="checkbox"/> Paid UF ID number <u>PD3006533</u> <input type="checkbox"/> Small business <input type="checkbox"/> Public health <input type="checkbox"/> Barrier-to-Innovation <input type="checkbox"/> Other (specify) <input type="checkbox"/> Orphan designation <input type="checkbox"/> No-fee 505(b)(2) (see NDA Regulatory Filing Review for instructions) <input type="checkbox"/> Other (specify)
❖ Application Integrity Policy (AIP)		
<ul style="list-style-type: none"> • Applicant is on the AIP • This application is on the AIP 		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

<ul style="list-style-type: none"> • Exception for review (Center Director's memo) 	<p>N/A</p>
<ul style="list-style-type: none"> • OC clearance for approval 	<p>N/A/</p>
<ul style="list-style-type: none"> • Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification & certifications from foreign applicants are cosigned by US agent. 	<p><input checked="" type="checkbox"/> Verified</p>
<p>❖ Patent</p>	<p style="background-color: #cccccc;"></p>
<ul style="list-style-type: none"> • Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. 	<p><input checked="" type="checkbox"/> Verified</p>
<ul style="list-style-type: none"> • Patent certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	<p>21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)</p>
<ul style="list-style-type: none"> • [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	<p></p>
<ul style="list-style-type: none"> • [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next box below (Exclusivity)).</i> • [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation. <p>Answer the following questions for each paragraph IV certification:</p> <p>(1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).</p> <p><i>If "Yes," skip to question (4) below. If "No," continue with question (2).</i></p> <p>(2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?</p> <p><i>If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).</i></p> <p><i>If "No," continue with question (3).</i></p> <p>(3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its</p>	<p><input checked="" type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>

representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).

If "No," continue with question (5).

- (5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).

If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).

If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.

❖ Exclusivity (approvals only)	
<ul style="list-style-type: none"> • Exclusivity summary • Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.) 	Enclosed; 3-years requested NO
<ul style="list-style-type: none"> • Is there existing orphan drug exclusivity protection for the "same drug" for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification. 	<input type="checkbox"/> Yes, Application # _____ <input checked="" type="checkbox"/> No
❖ Administrative Reviews (Project Manager, ADRA) (indicate date of each review)	Filing Review(s)

General Information	
Actions	
• Proposed action	(X) AP () TA () AE () NA
• Previous actions (specify type and date for each action taken)	This is the first action.
• Status of advertising (approvals only)	(X) Materials requested in AP letter () Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	(X) Yes () Not applicable
• Indicate what types (if any) of information dissemination are anticipated	() None (X) Press Release () Talk Paper () Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	Enclosed (draft of 3-15-07) <i>approval letter 4/12/07</i>
• Most recent applicant-proposed labeling	Enclosed (date)
• Original applicant-proposed labeling	Enclosed
• Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings (indicate dates of reviews and meetings)	3/23/07 13/21/07 DDMAC Waiting on Re-Review Write-up
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	N/A
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	
• Applicant proposed	Enclosed
• Reviews	See NDA 21-984 – Chemistry Review
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	None
• Documentation of discussions and/or agreements relating to post-marketing commitments	None
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	
	Enclosed
❖ Memoranda and Telecons	
	To be added
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	N/A
• Pre-NDA meeting (indicate date)	May 8, 2006
• Pre-Approval Safety Conference (indicate date; approvals only)	Not held yet
• Other	N/A
❖ Advisory Committee Meeting	
• Date of Meeting	No Meeting Held
• 48-hour alert	N/A
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	
	Not Applicable

Div Dir 4113
Office Dir 4112
y
9/15/07
4/11/07

Summary Application Review	
Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) (indicate date for each review)	To be added when available
Clinical Information	
❖ Clinical review(s) (indicate date for each review)	Draft Enclosed - Final 3/19/07
❖ Microbiology (efficacy) review(s) (indicate date for each review)	Draft Enclosed - Final
❖ Safety Update review(s) (indicate date or location if incorporated in another review)	See Clinical Review
❖ Risk Management Plan review(s) (indicate date/location if incorporated in another rev)	N/A
❖ Pediatric Page (separate page for each indication addressing status of all age groups)	Enclosed - 3/12/07
❖ Demographic Worksheet (NME approvals only)	N/A
❖ Statistical review(s) (indicate date for each review)	Final 3/14/07 - Enclosed
❖ Biopharmaceutical review(s) (indicate date for each review)	Final 3/08/07 - Enclosed
❖ Controlled Substance Staff review(s) and recommendation for scheduling (indicate date for each review)	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	Summary of (1) Enclosed - (1) pending Enclosed 3/30/07
• Bioequivalence studies	N/A
CMC Information	
❖ CMC review(s) (indicate date for each review)	Final 2/25/07 - Enclosed
❖ Environmental Assessment	
• Categorical Exclusion (indicate review date)	Requested/Granted/See Chemistry Review Page
• Review & FONSI (indicate date of review)	N/A
• Review & Environmental Impact Statement (indicate date of each review)	N/A
❖ Microbiology (validation of sterilization & product sterility) review(s) (indicate date for each review)	See Final review dated 6-15-06
❖ Facilities inspection (provide EER report)	Date completed: For date see page 6 of Chemistry Review (X) Acceptable () Withhold recommendation
❖ Methods validation	(X) Completed () Requested () Not yet requested
Nonclinical Pharmacology Information	
❖ Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	Final 2/2/07 - Enclosed
❖ Nonclinical inspection review summary	Not Applicable
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	Not Applicable
❖ CAC/ECAC report	Not Applicable

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

**PRESCRIPTION DRUG USER FEE
COVERSHEET**

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: <http://www.fda.gov/cder/pdufa/default.htm>

<p>1. APPLICANT'S NAME AND ADDRESS</p> <p>GLAXO GROUP LIMITED Jim McCarthy One Franklin Plaza 200 N. 16th Street Philadelphia PA 19101 US</p>	<p>4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER</p> <p>22-055</p>
<p>2. TELEPHONE NUMBER</p> <p>215-751-5923</p>	<p>5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?</p> <p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p> <p>IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:</p> <p><input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION</p> <p><input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:</p>

<p>3. PRODUCT NAME</p> <p>retapamulin</p>	<p>6. USER FEE I.D. NUMBER</p> <p>PD3006533</p>
---	---

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
<input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act	<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES NO

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services Food and Drug Administration CBER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448	Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 Rockville, MD 20852	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.
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<p>SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE</p> <p><i>David H. Gurbette</i></p>	<p>TITLE</p> <p>Vice President U.S. Regulatory Affairs</p>	<p>DATE</p> <p>May 25, 2006</p>
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9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION

\$767,400.00