

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

208945Orig1s000

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 208945 BLA # N/A	NDA Supplement # N/A BLA Supplement # N/A	If NDA, Efficacy Supplement Type: N/A (an action package is not required for SE8 or SE9 supplements)
Proprietary Name: Xepi Established/Proper Name: Ozenoxacin Cream Dosage Form: Cream; 10g, 30g, 45 g tubes		Applicant: Ferrer International, S.A. Agent for Applicant (if applicable): Prosoft Clinical
RPM: Eva Zuffova		Division: DAIP
NDA Application Type: ☒ 505(b)(1) ☐ 505(b)(2) Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2) BLA Application Type: ☐ 351(k) ☐ 351(a) Efficacy Supplement: ☐ 351(k) ☐ 351(a)		For ALL 505(b)(2) applications, two months prior to EVERY action: - Review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. - Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) ☐ No changes ☐ New patent/exclusivity (notify CDER OND IO) Date of check: <i>Note: If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</i>
❖ Actions		
- Proposed action - User Fee Goal Date is January 17, 2018		☒ AP ☐ TA ☐ CR
Previous actions (specify type and date for each action taken)		☒ None
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain		☐ N/A
❖ Application Characteristics ³		

¹ The Application Information Section is (only) a checklist. The Contents of Action Package Section (beginning on page 2) lists the documents to be included in the Action Package.

² For resubmissions, 505(b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA.

Review priority: ☒ Standard ☐ Priority
 Chemical classification (new NDAs only):
 (confirm chemical classification at time of approval)

- | | |
|---|---|
| ☐ Fast Track | ☐ Rx-to-OTC full switch |
| ☐ Rolling Review | ☐ Rx-to-OTC partial switch |
| ☐ Orphan drug designation | ☐ Direct-to-OTC |
| ☐ Breakthrough Therapy designation | |

(NOTE: Set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager;
 Refer to the "RPM BT Checklist for Considerations after Designation Granted" for other required actions: [CST SharePoint](#))

NDAs: Subpart H

- ☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)

Subpart I

- ☐ Approval based on animal studies

- ☐ Submitted in response to a PMR
☐ Submitted in response to a PMC
☐ Submitted in response to a Pediatric Written Request

BLAs: Subpart E

- ☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)

Subpart H

- ☐ Approval based on animal studies

- REMS: ☐ MedGuide
☐ Communication Plan
☐ ETASU
☐ MedGuide w/o REMS
☐ REMS not required

Comments:

❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (approvals only)	N/A
❖ Public communications (approvals only)	
• Office of Executive Programs (OEP) liaison has been notified of action	☐ Yes ☒ No
• Indicate what types (if any) of information were issued	☒ None ☐ FDA Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other
❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)?	☒ No ☐ Yes
• If so, specify the type	N/A
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
CONTENTS OF ACTION PACKAGE	
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (approvals only)	☐ Included
Documentation of consent/non-consent by officers/employees	☐ Included

Action Letters

❖ Copies of all action letters (including approval letter with final labeling)	Action(s) and date(s) 12-11-2017
Labeling	
❖ Package Insert (write submission/communication date at upper right of first page of PI)	
• Most recent draft labeling (if it is division-proposed labeling, it should be in track-changes format)	☒ Included
• Original applicant-proposed labeling	☒ Included
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (write submission/communication date at upper right of first page of each piece)	☐ Medication Guide ☐ Patient Package Insert ☐ Instructions for Use ☐ Device Labeling ☒ None
• Most-recent draft labeling (if it is division-proposed labeling, it should be in track-changes format)	☒ Included
• Original applicant-proposed labeling	☒ Included
❖ Labels (full color carton and immediate-container labels) (write submission/communication date on upper right of first page of each submission)	
• Most-recent draft labeling	☒ Included
❖ Proprietary Name	Granted: 4-25-2017 Denied: 1-30-2017 Denied: 10-24-2016
• Acceptability/non-acceptability letter(s) (indicate date(s)) • Review(s) (indicate date(s)) Xepi - 4-20-2017; (b) (4) - 1-27-2017; (b) (4) - 10-20-2016	
❖ Labeling reviews (indicate dates of reviews)	RPM: ☒ None 8-29-2016 DMEPA: ☒ None 5-22-2017; Memo: 11-30-2017 DMPP/PLT (DRISK): ☒ None OPDP: ☐ None 3-16-2017 SEALD: ☒ None CSS: ☒ None Product Quality ☒ None Other: ☒ None

Administrative / Regulatory Documents

❖ RPM Filing Review ⁴ /Memo of Filing Meeting (indicate date of each review)	8-16-2016
❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	☒ Not a (b)(2)
❖ NDAs/NDA supplements only: Exclusivity Summary (signed by Division Director)	☐ Completed (Do not include)
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
• Applicant is on the AIP	☐ Yes ☒ No

⁴ Filing reviews for scientific disciplines are NOT required to be included in the action package.

- This application is on the AIP - If yes, Center Director's Exception for Review memo (indicate date) - If yes, OC clearance for approval (indicate date of clearance communication)	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics (approvals only) - Date reviewed by PeRC _____ - If PeRC review not necessary, explain: _____	5-17-2017
❖ Breakthrough Therapy Designation	☒ N/A
Breakthrough Therapy Designation Letter(s) (granted, denied, an/or rescinded)	
CDER Medical Policy Council Breakthrough Therapy Designation Determination Review Template(s) (include only the completed template(s) and not the meeting minutes)	
CDER Medical Policy Council Brief – Evaluating a Breakthrough Therapy Designation for Rescission Template(s) (include only the completed template(s) and not the meeting minutes) (completed CDER MPC templates can be found in DARRTS as clinical reviews or on the MPC SharePoint Site)	
❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, Formal Dispute Resolution Request decisional letters, etc.) (do not include OPDP letters regarding pre-launch promotional materials as these are non-disclosable; do not include Master File letters; do not include previous action letters, as these are located elsewhere in package)	
❖ Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes)	
❖ Minutes of Meetings	
If not the first review cycle, any end-of-review meeting (indicate date of mtg)	☒ N/A or no mtg
Pre-NDA/BLA meeting (indicate date of mtg)	1-13-2016
EOP2 meeting (indicate date of mtg)	6-10-2011
Mid-cycle Communication (indicate date of mtg)	12-9-2016
Late-cycle Meeting (indicate date of mtg)	3-24-2017
Other milestone meetings (e.g., EOP2a, CMC focused milestone meetings) (indicate dates of mtgs)	
❖ Advisory Committee Meeting(s)	☒ No AC meeting
Date(s) of Meeting(s)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (indicate date for each review)	12-7-2107
Division Director Summary Review (indicate date for each review)	12-6-2017
Cross-Discipline Team Leader Review (indicate date for each review)	12-6-2017
PMR/PMC Development Templates (indicate total number)	☒ None
Clinical	

❖ Clinical Reviews	
• Clinical Team Leader Review(s) (indicate date for each review)	☒ No separate review
• Clinical review(s) (indicate date for each review)	3-27-2017
• Social scientist review(s) (if OTC drug) (indicate date for each review)	☒ None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☐ and include a review/memo explaining why not (indicate date of review/memo)	Page 91; clinical review
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (indicate date of each review) ⁵	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (indicate date of each review)	☒ N/A
❖ Risk Management • REMS Documents and REMS Supporting Document (indicate date(s) of submission(s)) • REMS Memo(s) and letter(s) (indicate date(s)) • Risk management review(s) and recommendations (including those by OSE and CSS) (indicate date of each review and indicate location/date if incorporated into another review)	N/A N/A 2-23-2017 Addendum: 12-1-2017
❖ OSI Clinical Inspection Review Summary(ies) (include copies of OSI letters to investigators)	OSI Summary: 2-14-2017 Letters included
Clinical Microbiology ☐ None	
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	☒ No separate review
Clinical Microbiology Review(s) (indicate date for each review)	3-22-2017
Biostatistics ☐ None	
❖ Statistical Division Director Review(s) (indicate date for each review)	☒ No separate review
Statistical Team Leader Review(s) (indicate date for each review)	☒ No separate review
Statistical Review(s) (indicate date for each review)	3-6-2017
Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	☒ No separate review
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	☒ No separate review
Clinical Pharmacology review(s) (indicate date for each review)	3-31-2017
❖ OSI Clinical Pharmacology Inspection Review Summary (include copies of OSI letters)	☒ None requested

⁵ For Part 3 combination products, all reviews from the reviewing Center(s) should be entered into the official archive (for further instructions, see "Section 508 Compliant Documents: Process for Regulatory Project Managers" located in the CST electronic repository).

Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	☒ No separate review
• Supervisory Review(s) (indicate date for each review)	☒ No separate review
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	3-21-2017
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	☒ None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	☒ No carc
❖ ECAC/CAC report/memo of meeting	☒ None
❖ OSI Nonclinical Inspection Review Summary (include copies of OSI letters)	☒ None requested
Product Quality ☐ None	
❖ Product Quality Discipline Reviews ⁶	
• Tertiary review (indicate date for each review)	☒ None
• Secondary review (e.g., Branch Chief) (indicate date for each review)	☐ None Orig. Rev. 3-9-2017
• Integrated Quality Assessment (contains the Executive Summary and the primary reviews from each product quality review discipline) (indicate date for each review)	☐ None Orig. Rev.: 3-9-2017 Addendum: 6-7-2017 Review #2: 12-1-2017
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team (indicate date of each review)	☒ None
❖ Environmental Assessment (check one) (original and supplemental applications)	
☒ Categorical Exclusion (indicate review date)(all original applications and all efficacy supplements that could increase the patient population)	3-9-2017; Pg. 59
☐ Review & FONSI (indicate date of review)	
☐ Review & Environmental Impact Statement (indicate date of each review)	
❖ Facilities Review/Inspection	
☐ Facilities inspections (indicate date of recommendation; within one week of taking an approval action, confirm that there is an acceptable recommendation before issuing approval letter) (only original applications and efficacy supplements that require a manufacturing facility inspection(e.g., new strength, manufacturing process, or manufacturing site change)	☐ Acceptable ☒ Withhold recommendation ☐ Not applicable

⁶ Do not include Master File (MF) reviews or communications to MF holders. However, these documents should be made available upon signatory request.

Day of Approval Activities

❖ For all 505(b)(2) applications:	☐ No changes
• Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)	☐ New patent/exclusivity (Notify CDER OND IO)
• Finalize 505(b)(2) assessment	☐ Done
❖ For Breakthrough Therapy (BT) Designated drugs:	☐ Done
• Notify the CDER BT Program Manager	(Send email to CDER OND IO)
❖ For products that need to be added to the flush list (generally opioids): <u>Flush List</u>	☐ Done
• Notify the Division of Online Communications, Office of Communications	
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	☐ Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	☐ Done
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the "preferred" name	☐ Done
❖ Ensure Pediatric Record is accurate	☐ Done
❖ Send approval email within one business day to CDER-APPROVALS	
❖ Take Action Package (if in paper) down to Document Room for scanning within two business days	

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 208945 BLA # N/A	NDA Supplement # N/A BLA Supplement # N/A	If NDA, Efficacy Supplement Type: N/A <i>(an action package is not required for SE8 or SE9 supplements)</i>
Proprietary Name: Xepi Established/Proper Name: Ozenoxacin Cream Dosage Form: Cream; 10g, 30g, 45 g tubes		Applicant: Ferrer International, S.A. Agent for Applicant (if applicable): Prosoft Clinical
RPM: Eva Zuffova		Division: DAIP
NDA Application Type: ☒ 505(b)(1) ☐ 505(b)(2) Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2) BLA Application Type: ☐ 351(k) ☐ 351(a) Efficacy Supplement: ☐ 351(k) ☐ 351(a)		<u>For ALL 505(b)(2) applications, two months prior to EVERY action:</u> Review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) ☐ No changes ☐ New patent/exclusivity <i>(notify CDER OND IO)</i> Date of check: <i>Note: If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</i>
❖ Actions		
- Proposed action - User Fee Goal Date is June 22, 2017		☐ AP ☐ TA ☒ CR
Previous actions <i>(specify type and date for each action taken)</i>		☒ None
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain		☐ N/A
❖ Application Characteristics ³		

¹ The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 2) lists the documents to be included in the Action Package.

² For resubmissions, 505(b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA.

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only):
(confirm chemical classification at time of approval)

- | | |
|---|---|
| ☐ Fast Track | ☐ Rx-to-OTC full switch |
| ☐ Rolling Review | ☐ Rx-to-OTC partial switch |
| ☐ Orphan drug designation | ☐ Direct-to-OTC |
| ☐ Breakthrough Therapy designation | |

(NOTE: Set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager;
Refer to the "RPM BT Checklist for Considerations after Designation Granted" for other required actions: [CST SharePoint](#))

NDAs: Subpart H

- ☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)

Subpart I

- ☐ Approval based on animal studies

- ☐ Submitted in response to a PMR
☐ Submitted in response to a PMC
☐ Submitted in response to a Pediatric Written Request

BLAs: Subpart E

- ☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)

Subpart H

- ☐ Approval based on animal studies

- REMS: ☐ MedGuide
☐ Communication Plan
☐ ETASU
☐ MedGuide w/o REMS
☐ REMS not required

Comments:

❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (approvals only)	N/A
❖ Public communications (approvals only)	
• Office of Executive Programs (OEP) liaison has been notified of action	☐ Yes ☒ No
• Indicate what types (if any) of information were issued	☒ None ☐ FDA Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other
❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)?	☒ No ☐ Yes
• If so, specify the type	N/A
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
CONTENTS OF ACTION PACKAGE	
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (approvals only)	☐ Included
Documentation of consent/non-consent by officers/employees	☐ Included

Action Letters	
❖ Copies of all action letters (including approval letter with final labeling)	Action(s) and date(s) 6-22-2017
Labeling	
❖ Package Insert (write submission/communication date at upper right of first page of PI)	
Most recent draft labeling (if it is division-proposed labeling, it should be in track-changes format)	☒ Included
Original applicant-proposed labeling	☒ Included
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (write submission/communication date at upper right of first page of each piece)	☐ Medication Guide ☐ Patient Package Insert ☐ Instructions for Use ☐ Device Labeling ☒ None
Most-recent draft labeling (if it is division-proposed labeling, it should be in track-changes format)	☒ Included
Original applicant-proposed labeling	☒ Included
❖ Labels (full color carton and immediate-container labels) (write submission/communication date on upper right of first page of each submission)	
Most-recent draft labeling	☒ Included
❖ Proprietary Name - Acceptability/non-acceptability letter(s) (indicate date(s)) - Review(s) (indicate date(s)) Xepi - 4-20-2017; (b) (4) - 1-27-2017; (b) (4) - 10-20-2016	Granted: 4-25-2017 Denied: 1-30-2017 Denied: 10-24-2016
❖ Labeling reviews (indicate dates of reviews)	RPM: ☒ None 8-29-2016 DMEPA: ☒ None 5-19-2017 DMPP/PLT (DRISK): ☒ None OPDP: ☐ None 3-16-2017 SEALD: ☒ None CSS: ☒ None Product Quality ☒ None Other: ☒ None
Administrative / Regulatory Documents	
❖ RPM Filing Review ⁴ /Memo of Filing Meeting (indicate date of each review)	8-16-2016
❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	☒ Not a (b)(2)
❖ NDAs/NDA supplements only: Exclusivity Summary (signed by Division Director)	☐ Completed (Do not include)
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
Applicant is on the AIP	☐ Yes ☒ No

⁴ Filing reviews for scientific disciplines are NOT required to be included in the action package.

- This application is on the AIP - If yes, Center Director's Exception for Review memo <i>(indicate date)</i> - If yes, OC clearance for approval <i>(indicate date of clearance communication)</i>	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics <i>(approvals only)</i> Date reviewed by PeRC _____ If PeRC review not necessary, explain: _____	5-17-2017
❖ Breakthrough Therapy Designation	☒ N/A
Breakthrough Therapy Designation Letter(s) (granted, denied, an/or rescinded)	
CDER Medical Policy Council Breakthrough Therapy Designation Determination Review Template(s) <i>(include only the completed template(s) and not the meeting minutes)</i>	
CDER Medical Policy Council Brief – Evaluating a Breakthrough Therapy Designation for Rescission Template(s) <i>(include only the completed template(s) and not the meeting minutes)</i> <i>(completed CDER MPC templates can be found in DARRTS as clinical reviews or on the MPC SharePoint Site)</i>	
❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, Formal Dispute Resolution Request decisional letters, etc.) <i>(do not include OPDP letters regarding pre-launch promotional materials as these are non-disclosable; do not include Master File letters; do not include previous action letters, as these are located elsewhere in package)</i>	
❖ Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes)	
❖ Minutes of Meetings	
If not the first review cycle, any end-of-review meeting <i>(indicate date of mtg)</i>	☒ N/A or no mtg
Pre-NDA/BLA meeting <i>(indicate date of mtg)</i>	1-13-2016
EOP2 meeting <i>(indicate date of mtg)</i>	6-10-2011
Mid-cycle Communication <i>(indicate date of mtg)</i>	12-9-2016
Late-cycle Meeting <i>(indicate date of mtg)</i>	3-24-2017
Other milestone meetings (e.g., EOP2a, CMC focused milestone meetings) <i>(indicate dates of mtgs)</i>	
❖ Advisory Committee Meeting(s)	☒ No AC meeting
Date(s) of Meeting(s)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo <i>(indicate date for each review)</i>	6-22-2107
Division Director Summary Review <i>(indicate date for each review)</i>	6-21-2017
Cross-Discipline Team Leader Review <i>(indicate date for each review)</i>	6-14-2017
PMR/PMC Development Templates <i>(indicate total number)</i>	☒ None
Clinical	

❖ Clinical Reviews		
• Clinical Team Leader Review(s) (indicate date for each review)		☒ No separate review
• Clinical review(s) (indicate date for each review)		3-27-2017
• Social scientist review(s) (if OTC drug) (indicate date for each review)		☒ None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☐ and include a review/memo explaining why not (indicate date of review/memo)		Page 91; clinical review
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (indicate date of each review) ⁵		☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (indicate date of each review)		☒ N/A
❖ Risk Management - REMS Documents and REMS Supporting Document (indicate date(s) of submission(s)) - REMS Memo(s) and letter(s) (indicate date(s)) - Risk management review(s) and recommendations (including those by OSE and CSS) (indicate date of each review and indicate location/date if incorporated into another review)		N/A N/A 2-23-2017
❖ OSI Clinical Inspection Review Summary(ies) (include copies of OSI letters to investigators)		OSI Summary: 2-14-2017 Letters included
Clinical Microbiology ☐ None		
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)		☒ No separate review
Clinical Microbiology Review(s) (indicate date for each review)		3-22-2017
Biostatistics ☐ None		
❖ Statistical Division Director Review(s) (indicate date for each review)		☒ No separate review
Statistical Team Leader Review(s) (indicate date for each review)		☒ No separate review
Statistical Review(s) (indicate date for each review)		3-6-2017
Clinical Pharmacology ☐ None		
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)		☒ No separate review
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)		☒ No separate review
Clinical Pharmacology review(s) (indicate date for each review)		3-31-2017
❖ OSI Clinical Pharmacology Inspection Review Summary (include copies of OSI letters)		☒ None requested

⁵ For Part 3 combination products, all reviews from the reviewing Center(s) should be entered into the official archive (for further instructions, see “Section 508 Compliant Documents: Process for Regulatory Project Managers” located in the CST electronic repository).

Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	☒ No separate review
• Supervisory Review(s) (indicate date for each review)	☒ No separate review
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	3-21-2017
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	☒ None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	☒ No carc
❖ ECAC/CAC report/memo of meeting	☒ None
❖ OSI Nonclinical Inspection Review Summary (include copies of OSI letters)	☒ None requested
Product Quality ☐ None	
❖ Product Quality Discipline Reviews ⁶	
• Tertiary review (indicate date for each review)	☒ None
• Secondary review (e.g., Branch Chief) (indicate date for each review)	☐ None Orig. Rev. 3-9-2017
• Integrated Quality Assessment (contains the Executive Summary and the primary reviews from each product quality review discipline) (indicate date for each review)	☐ None Orig. Rev. 3-9-2017 Addendum: 6-7-2017
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team (indicate date of each review)	☒ None
❖ Environmental Assessment (check one) (original and supplemental applications)	
☒ Categorical Exclusion (indicate review date)(all original applications and all efficacy supplements that could increase the patient population)	3-9-2017; Pg. 59
☐ Review & FONSI (indicate date of review)	
☐ Review & Environmental Impact Statement (indicate date of each review)	
❖ Facilities Review/Inspection	
☐ Facilities inspections (indicate date of recommendation; within one week of taking an approval action, confirm that there is an acceptable recommendation before issuing approval letter) (only original applications and efficacy supplements that require a manufacturing facility inspection(e.g., new strength, manufacturing process, or manufacturing site change)	☐ Acceptable ☒ Withhold recommendation ☐ Not applicable

⁶ Do not include Master File (MF) reviews or communications to MF holders. However, these documents should be made available upon signatory request.

Day of Approval Activities	
❖ For all 505(b)(2) applications: Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)	☐ No changes ☐ New patent/exclusivity <i>(Notify CDER OND IO)</i>
Finalize 505(b)(2) assessment	☐ Done
❖ For Breakthrough Therapy (BT) Designated drugs: Notify the CDER BT Program Manager	☐ Done <i>(Send email to CDER OND IO)</i>
❖ For products that need to be added to the flush list (generally opioids): Flush List Notify the Division of Online Communications, Office of Communications	☐ Done
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	☐ Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	☐ Done
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name	☐ Done
❖ Ensure Pediatric Record is accurate	☐ Done
❖ Send approval email within one business day to CDER-APPROVALS	
❖ Take Action Package (if in paper) down to Document Room for scanning within two business days	

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

/s/

EVA ZUFFOVA
06/22/2017

From: Zuffova, Eva
Sent: Monday, March 13, 2017 12:06 PM
To: Bob Babilon
Cc: Rivera, Luz E (CDER)
Subject: RE: Clarification request: INFORMATION REQUEST NDA 208945

Good afternoon Robert,
below please see response to the clarification request sent by the Sponsor on March 9, 2017.

(b) (4)

Acceptability of the submitted BCC assay protocol is subject to review and evaluation of the validation data, when provided.

Please note that, as conveyed earlier, your response to the microbiology deficiencies submitted in the amendment dated February 24, 2017 is still under review."

Sincerely,
Eva

Eva Zuffova, PhD, MS
Regulatory Health Project Manager (RPM)
Division of Anti-Infective Products (DAIP)
Office of Antimicrobial Products (OAP)
Center for Drug Evaluation and Research (CDER)
Building 22, Room 6395
Silver Spring, MD 20993
Telephone: (301) 796-0697

-----Original Message-----

From: Bob Babilon [mailto:B.Babilon@prosoftclinical.com]
Sent: Thursday, March 09, 2017 10:27 AM
To: Rivera, Luz E (CDER); Zuffova, Eva
Cc: Bob Babilon
Subject: Clarification request: INFORMATION REQUEST NDA 208945

Drs. Rivera and Zuffova:

In preparing responses to the most recent CMC requests, the sponsor has indicated that some clarification should be requested:

Under Product Quality Microbiology, the request is:

"We acknowledge receipt of your response to the microbiology deficiencies submitted in the amendment dated February 24, 2017. We are still in the process of reviewing the information but we wanted to convey to you that we will need actual validation data from the proposed Burkholderia cepacia complex assay."

Sponsor has stated that, as provided in the February 24, 2017 (SN0008) Response to FDA Request submission, under 1.11.1 "Protocols for BCC Testing", document section 7.0.

(b) (4)

(b) (4)

Thank you in advance for your response:

Robert Babilon MS MBA
Vice President
Regulatory Affairs and Quality Assurance
Prosoft Clinical
Office: (484) 320-2068
Cell: (b) (6)
Fax: (484) 580 8165
b.babilon@prosoftclinical.com
www.prosoftclinical.com

Prosoft Clinical is a Pharmaceutical product design and development organization with CRO capabilities for full services, including CMC and regulatory consulting, data management, statistical programming and analysis, clinical project management and site monitoring, medical writing, eDC, eDiary etc. Since 1995, Prosoft Clinical has been providing services to the Pharmaceutical, Biotech, and Medical Device industries in many therapeutic areas.

The contents of this transmission may contain information that is proprietary, privileged, confidential, or otherwise is legally exempt from disclosure. This e-mail solely is intended for the use of the recipient(s) identified above. If you are not an intended recipient, you may not review, disseminate, distribute or duplicate this e-mail or any attachment. If you are not an intended recipient, please contact the sender by reply e-mail and delete this message.

-----Original Message-----

From: DoNotReply@fda.hhs.gov [mailto:DoNotReply@fda.hhs.gov]

Sent: Tuesday, March 7, 2017 6:01 PM

To: Bob Babilon <B.Babilon@prosoftclinical.com>

Cc: luz.e.rivera@fda.hhs.gov; Eva.Zuffova@fda.hhs.gov

Subject: INFORMATION REQUEST NDA 208945

NDA 208945

INFORMATION REQUEST

Prosoft Clinical

Attention: Robert W. Babilon, MS, MBA, VP, Regulatory Affairs and Quality Assurance US Agent for Ferrer Internacional, S.A. in Spain

996 Old Eagle School Road, Suite 1106

Wayne, PA 19087

Dear Mr. Babilon:

Please find attached the information request letter for NDA 208945.

We request a written response by Monday, March 27, 2017. Please provide your response via email followed by an official submission to the NDA.

We request that you acknowledge this communication upon receipt.

Best regards,

LCDR Luz E Rivera, Psy.D.

Quality Assessment Lead (Acting), Div. I, Branch I Office of Program and Regulatory Operations Office of Pharmaceutical Quality Center for Drug Evaluation and Research

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

/s/

EVA ZUFFOVA
06/14/2017

PeRC Meeting Minutes
May 17, 2017

PeRC Members Attending:

Skip Nelson
Meshaun Payne
Jacqueline Yancy
Hari Cheryl Sachs
Wiley Chambers
Susan McCune
Tom Smith
Gil Burkhart
Donna Snyder
Kevin Krudys
Lily Mulugeta
Shrikant Pegay
Dionna Green
Rosemary Addy
Jingjing Ye
James Travis
Mark Rothmann

Agenda

	NON-RESPONSIVE				
9:00					
9:50					
10:00					
10:20					
10:35	NDA 208945	Ozenoxacin Cream 1% (Partial Waiver/Assessment)	DAIP	Eva Zuffova	Topical treatment of impetigo in adults, adolescents, children (b) (4) 2 months and older
	NON-RESPONSIVE				
10:50					
11:10					
11:20					

3 Page(s) has been Withheld in Full as NON-RESPONSIVE immediately following this page

NON-RESPONSIVE

Ozenoxacin Cream 1% (Partial Waiver/Assessment)

- Proposed Indication: Topical treatment of impetigo in adults, adolescents, children (b) (4) 2 months and older due to *Staphylococcus aureus* and *Streptococcus pyogenes*.

- This product triggers PREA as a new indication, dosage form, dosing regimen and route of administration.
- This product has a PDUFA goal date of June 22, 2017.
- The sponsor plans to request a partial waiver in pediatrics less than 2 months as studies are impossible or highly impracticable.
- The sponsor completed 2 well controlled trials with a 15% treatment difference over placebo in pediatrics 2 months to 17 years of age.
- The division states that it will get a CR for chemistry issues but will continue with the review of the label so that when it is resubmitted it will be ready to approve. The product will be labeled for 2 months and above and waive less than 2 months.
- *PeRC Recommendations:*
 - o The PeRC agrees to partial waiver in pediatrics less than 2 months as studies are impossible or highly impracticable.
 - o The PeRC agrees that the product can be labeled for pediatrics 2 months to 17 years.

NON-RESPONSIVE

3 Page(s) has been Withheld in Full as NON-RESPONSIVE immediately following this page

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

/s/

JACQUILINE A YANCY
06/07/2017



NDA 208945

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Ferrer Internacional, S.A.
c/o Prosoft Clinical
996 Old Eagle School Road, Suite 1106
Wayne, PA 19087

ATTENTION: Robert W. Babilon, MS, MBA
Vice President, Regulatory Affairs and Quality Assurance

Dear Mr. Babilon:

Please refer to your New Drug Application (NDA) dated and received June 23, 2016, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ozenoxacin Cream, 1%.

We also refer to your correspondence, dated and received March 6, 2017, requesting review of your proposed proprietary name, Xepi.

We have completed our review of the proposed proprietary name, Xepi and have concluded that it is conditionally acceptable.

If any of the proposed product characteristics as stated in your March 6, 2017, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review. Additionally, if your application receives a complete response, a new request for name review for your proposed name should be submitted when you respond to the application deficiencies.

If you require information on submitting requests for proprietary name review or PDUFA performance goals associated with proprietary name reviews, we refer you to the following:

- Guidance for Industry Contents of a Complete Submission for the Evaluation of Proprietary Names
(<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf>)
- PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017,
(<http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf>)

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Janet G. Higgins, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (240) 402-0330. For any other information regarding this application, contact Eva Zuffova, Regulatory Project Manager in the Office of New Drugs, at (301) 796-0697.

Sincerely,

{See appended electronic signature page}

Todd Bridges, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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

/s/

DANIELLE M HARRIS on behalf of TODD D BRIDGES
04/25/2017

From: Zuffova, Eva
Sent: Thursday, February 02, 2017 7:43 AM
To: 'Bob Babilon'
Subject: NDA 208945 ozenoxacin - information request

Good morning Bob,
below please find information request from our microbiology product quality review group.

These are minor deficiencies to be addressed by sponsor no later than within 3 weeks from today.

Comments:

1. [REDACTED] (b) (4)
[REDACTED]
2. The proposal to perform microbial limit test validation study [REDACTED] (b) (4) is acknowledged. As previously requested, please provide test methods and acceptance criteria to demonstrate the drug product is free of BCC. Your test method should be validated and a discussion of those methods should be provided. Test method validation should address multiple strains of the species and cells should be acclimated to the conditions in the manufacturing environment (e.g., temperature) before testing. Your submission should describe the preconditioning step (time, temperature, and solution(s) used), the total number of inoculated organisms, and the detailed test method to include growth medium and incubation conditions. It is essential that sufficient preconditioning of the organisms occurs during these method validation studies to ensure that the proposed recovery methods are adequate to recover organisms potentially present in the environment.
3. Due to the potential risk of contamination with organisms in the *Burkholderia cepacia* complex (BCC), the non-sterile [REDACTED] (b) (4) drug product release specification must include BCC testing. Therefore, please provide the test methods, acceptance criteria and validation results for BCC testing in the finished drug product. Please also provide updated release specifications for the finished drug product.
4. With regard to the microbial limits testing-
 - a. It is noted that the Microbial Validation Report states that "Since by nature Ozenoxacin is extremely effective against bacteria, total plate count and microorganism tests will be removed" (see P.5.3. Attachment 4, p14/15). Please clarify the circumstances in which the total plate count and microbial testing will not be performed.
 - b. Please provide the number of units and amounts used for routine testing.

5. [REDACTED] (b) (4)

Confirm that you have received this e-mail and let me know if you have any questions.
Eva

Eva Zuffova, PhD, MS

Regulatory Health Project Manager (RPM)
Division of Anti-Infective Products (DAIP)
Office of Antimicrobial Products (OAP)
Center for Drug Evaluation and Research (CDER)
Building 22, Room 6395
Silver Spring, MD 20993
Telephone: (301) 796-0697

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

/s/

EVA ZUFFOVA
02/07/2017



NDA 208945

**PROPRIETARY NAME REQUEST
UNACCEPTABLE**

Ferrer Internacional S.A.
c/o Prosoft Clinical
996 Old Eagle School Road, Suite 1106
Wayne, PA 19087

ATTENTION: Robert W. Babilon, MS, MBA
Vice President, Regulatory Affairs and Quality Assurance

Dear Mr. Babilon:

Please refer to your New Drug Application (NDA) dated and received on June 23, 2016, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ozenoxacin Cream, 1%.

We also refer to your dated and received November 3, 2016 correspondence, requesting a review of your proposed proprietary name, (b) (4).

We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons:

(b) (4)

We note that you have not proposed an alternate proprietary name for review. If you intend to have a proprietary name for this product, we recommend that you submit a new request for a proposed proprietary name review.

If you require additional information on developing proprietary names for drugs, proposing alternative proprietary names for consideration, or requesting reconsideration of our decision, we refer you to the following:

- Draft Guidance for Industry Best Practices in Developing Proprietary Names for Drugs, (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM398997.pdf>)
- Guidance for Industry Contents of a Complete Submission for the Evaluation of Proprietary Names (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf>)
- PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017, (<http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf>)

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Janet Higgins, Safety Regulatory Project Manager in the Office of

Surveillance and Epidemiology, at (240) 402-0330. For any other information regarding this application, contact Eva Zuffova, PhD, MS, Regulatory Project Manager, in the Office of New Drugs at (301) 796-0697.

Sincerely,

{See appended electronic signature page}

Todd Bridges, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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

/s/

DANIELLE M HARRIS on behalf of TODD D BRIDGES
01/30/2017



NDA 208945

MID-CYCLE COMMUNICATION

Ferrer Internacional S.A.
c/o Prosoft Clinical
Attention: Robert W. Babilon, MS, MBA
Vice President, Regulatory Affairs and Quality Assurance
996 Old Eagle School Road, Suite 1106
Wayne, PA 19087

Dear Mr. Babilon:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ozenoxacin Cream, 1%.

We also refer to the teleconference between representatives of your firm and the FDA on December 9, 2016. The purpose of the teleconference was to provide you an update on the status of the review of your application.

A record of the teleconference is enclosed for your information.

If you have any questions, call Eva Zuffova, PhD, MS, Regulatory Health Project Manager at (301) 796-0697.

Sincerely,

{See appended electronic signature page}

Thomas Smith, MD
Cross Discipline Team Leader
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure:
Mid-Cycle Communication



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MID-CYCLE COMMUNICATION

Meeting Date and Time: December 9, 2016

Application Number: NDA 208945

Product Name: Ozenoxacin Cream, 1%

Indication: Topical treatment of impetigo in adults, adolescents, children (b) (4)
2 months and older

Applicant Name: Ferrer International, S.A.

Meeting Chair: Thomas Smith, MD

Meeting Recorder: Eva Zuffova, PhD, MS

FDA ATTENDEES

Division of Anti-Infective Products

Carmen DeBellas, PharmD, RPh	Chief Regulatory Project Management
Tamara Feldblyum, MS, PhD	Clinical Microbiology Team Leader (Acting)
Avery Goodman, PhD	Clinical Microbiology Reviewer*
Seong Jang, PharmD	Clinical Pharmacology Team Leader*
Dorota Matecka, PhD	Product Quality Team Leader (Acting)
Karen Higgins, ScD	Statistical Team Leader
Christopher Kadoorie, PhD	Statistical Reviewer
Sumathi Nambiar, MD, MPH	Director
Terry Miller, PhD	Pharmacology/Toxicology Team Leader (Acting)
Thomas Smith, MD	Cross Discipline Team Leader
Xiaohui Wei, PhD	Clinical Pharmacology Reviewer
Eva Zuffova, PhD, MS	Regulatory Health Project Manager

Office of Antimicrobial Products

John Farley, MD, MPH	Deputy Director
----------------------	-----------------

Office of Product Quality

David Anderson, PhD	Product Quality Reviewer
Christina Capacci-Daniel, PhD	Product Quality Reviewer*

Office of Scientific Investigations

Sharon Gershon, PharmD	Good Clinical Practice Reviewer*
------------------------	----------------------------------

Office of Surveillance and Epidemiology

Janet Higgins	Senior Regulatory Health Project Manager
Deborah Myers, RPh, MBA	Safety Evaluator*
Till Olickal, PhD, PharmD	Risk Management Analyst

Eastern Research Group

Pegga Khorrami

Independent Assessor *

* Via teleconference

APPLICANT ATTENDEES

Ferrer Internacional, S.A.

Núria Albareda

Cristina Casado

Fabiana D'Aniello

José Ignacio Escamilla

Marta Fernández

Sergio González

Pablo Martín

Silvia Martín

Clinical Development

Regulatory Affairs

Project Director

Formulation Development Scientist

Analytical Development

Manager Analytical Development

Head of Pharmaceutical Development

Corporate Director, Regulatory Affairs & Compliance

Ferrer Consultants

Michelle Aquino

Robert Babilon

(b) (4)

(b) (4)

Donna Heren

(b) (4)

Noah Rosenberg

Sandy Roth

Associate, Regulatory Affairs and Quality Assurance,
Medimetrics

US Liaison, Prosoft Clinical

Director, (b) (4)

Regulatory Affairs, (b) (4)

Vice President Regulatory Affairs and Quality Assurance,
Medimetrics

Chief Executive Officer, (b) (4)

Chief Medical Officer, Medimetrics

Director, Clinical Development, Medimetrics

1.0 INTRODUCTION

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may or may not be able to consider your response before we take an action on your application during this review cycle.

2.0 SIGNIFICANT ISSUES

There are substantive review issues related to manufacturing facility deficiencies. Per 21 CFR 314.125, all manufacturing and testing processes must be adequate to preserve the identity, strength, quality, purity, and stability of the material produced and the proposed facilities must comply with the current good manufacturing practice regulations.

3.0 INFORMATION REQUESTS

There are no information requests at this time.

4.0 MAJOR SAFETY CONCERNS/RISK MANAGEMENT (REMS)

There are no major safety concerns identified at this time and there is currently no need for a REMS.

5.0 ADVISORY COMMITTEE MEETING

There are no plans at this time for an Advisory Committee meeting.

6.0 LATE-CYCLE MEETING (LCM) /OTHER PROJECTED MILESTONES

- | | |
|--|----------------|
| • INTERNAL LCM: | March 3, 2017 |
| • LCM Briefing Package due to the applicant | March 11, 2017 |
| • LATE-CYCLE Communication (Teleconference with Sponsor) | March 24, 2017 |

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

/s/

THOMAS D SMITH
01/04/2017

From: Zuffova, Eva [<mailto:Eva.Zuffova@fda.hhs.gov>]
Sent: Wednesday, October 26, 2016 10:54 AM
To: Bob Babilon <B.Babilon@prosoftclinical.com>
Subject: NDA 208945 - Container and carton label comments

Hi Bob,

For your convenience, below are the container and carton label recommendations to Ferrer:

RECOMMENDATIONS FOR the applicant.

We recommend the following be implemented prior to approval of this NDA 208945: All Container labels and Carton labeling (both trade and professional samples)

1. To prevent wrong route of administration medication error, revise the statement “(b) (4)” to read “Not For Ophthalmic, Oral, or Intravaginal Use.” This statement should be less prominent and on a single line (space permitting) below the statement “For Topical Use Only”. The statement “For Topical Use Only” should be more prominent (bolded and/or color font).

Container labels and Carton labeling (trade)

1. The drug barcode is often used as an additional verification before drug administration in the inpatient setting; therefore it is an important safety feature that should be part of the label whenever possible. We note that there is a space denoted for the bar code, however it is not included. Therefore, we request that you add the product barcode to each individual (trade) container labels and carton labeling as required per 21CFR 201.25(c)(2) and submit for our review.

Carton Labeling (professional samples)

1. The professional sample carton labeling currently submitted does not contain notation of where the lot number and expiration date are intended to be printed. The lot number statement is required on the immediate container per 21 CFR 201.10(i)(1) and the expiration date is required on the immediate container per 21 CFR 201.17. When determining this placement, please ensure that there are no other numbers located in close proximity to the lot number/expiration date where it can be mistaken as the lot number/expiration date.
2. The professional sample container label of one tube and the carton labeling of 4 tubes have the same NDC numbers. One carton containing more than one unit should have a different NDC number. Consider revising the NDC numbers so that the carton labeling and container label NDC package code numbers (last 2 digits) are different for these two package configurations.
3. The trade carton labeling includes the “Usual Dose: A thin layer should be applied to affected area twice daily for 5 days.” However, the professional sample carton labeling does not include the usual dose. Revise the professional sample carton labeling to include the statement, “Usual Dose: A thin layer should be applied to affected area twice daily for 5 days.”

Let me k now if you have questions,
Eva

Eva Zuffova, PhD, MS
Regulatory Health Project Manager (RPM)
Division of Anti-Infective Products (DAIP)
Office of Antimicrobial Products (OAP)
Center for Drug Evaluation and Research (CDER)
Building 22, Room 6395
Silver Spring, MD 20993
Telephone: (301) 796-0697

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

/s/

EVA ZUFFOVA
11/16/2016



NDA 208945

**PROPRIETARY NAME REQUEST
UNACCEPTABLE**

Ferrer Internacional S.A.
c/o Prosoft Clinical
996 Old Eagle School Road, Suite 1106
Wayne, PA 19087

ATTENTION: Robert W. Babilon, MS, MBA
Vice President, Regulatory Affairs and Quality Assurance

Dear Mr. Babilon:

Please refer to your New Drug Application (NDA) dated and received on June 23, 2016, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ozenoxacin Cream, 1%.

We also refer to your correspondence, dated and received July 29, 2016, requesting review of your proposed proprietary name, (b) (4)

We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons:

(b) (4)

- Draft Guidance for Industry Best Practices in Developing Proprietary Names for Drugs, (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM398997.pdf>)
- Guidance for Industry Contents of a Complete Submission for the Evaluation of Proprietary Names (<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf>)
- PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017, (<http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf>)

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Janet Higgins, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (240) 402-0330. For any other information regarding this application, contact Eva Zuffova, PhD, MS, Regulatory Project Manager, in the Office of New Drugs at (301) 796-0697.

Sincerely,

{See appended electronic signature page}

Todd Bridges, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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

/s/

IRENE Z CHAN on behalf of TODD D BRIDGES
10/24/2016

Zuffova, Eva

Subject: FW: NDA 208945 - ozenoxacin cream - report forms request
Attachments: Random_Sample_N208945_818.xls

From: Zuffova, Eva
Sent: Friday, August 19, 2016 1:13 PM
To: 'Bob Babilon'
Subject: NDA 208945 - ozenoxacin cream - report forms request

Hi Bob,
Please ask the applicant to provide the case report forms for the patients in the attached file.
Eva

Eva Zuffova, PhD, MS
Regulatory Health Project Manager (RPM)
Division of Anti-Infective Products (DAIP)
Office of Antimicrobial Products (OAP)
Center for Drug Evaluation and Research (CDER)
Building 22, Room 6395
Silver Spring, MD 20993
Telephone: (301) 796-0697

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

/s/

EVA ZUFFOVA
08/30/2016

From: Zuffova, Eva
Sent: Tuesday, August 30, 2016 9:35 AM
To: 'Bob Babilon'
Subject: NDA 208945 - Ozenoxacin - Information Request

Hi Bob,

Please convey the following statistical comments regarding NDA 208945 submission to the applicant.

1. We recommend that a brief algorithm is provided for primary and secondary analyses. The algorithm should clarify how analysis findings were derived (e.g. the datasets and variables used) so that possible discrepancies between Sponsor and Agency findings are minimized.
2. Subgroup analyses investigating efficacy and safety were not conducted by age, gender and race.

Note: these are not filling issues.

Eva Zuffova, PhD, MS
Regulatory Health Project Manager (RPM)
Division of Anti-Infective Products (DAIP)
Office of Antimicrobial Products (OAP)
Center for Drug Evaluation and Research (CDER)
Building 22, Room 6395
Silver Spring, MD 20993
Telephone: (301) 796-0697

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

/s/

EVA ZUFFOVA
08/30/2016



IND 105567

MEETING MINUTES

Ferrer Internacional S.A.
c/o AAIPharma Services Corporation.
Attention: Colleen M. Johns, RA Senior Analyst
2320 Scientific Park Drive
Wilmington, NC 28405

Dear Ms. Johns:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for ozenoxacin Cream.

We also refer to the meeting between representatives of your firm and the FDA on June 10, 2011. The purpose of the meeting was to discuss the development of this product. .

A copy of the official minutes of the meeting is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Fariba Izadi, Pharm.D., Regulatory Health Project Manager at (301) 796-0563.

Sincerely,

{See appended electronic signature page}

John Farley, MD, MPH
Acting Division Director
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE:
Meeting Minutes

MEMORANDUM OF MEETING MINUTES

Meeting Type: Type B
Meeting Category: End of Phase 2
Meeting Date and Time: June 10, 2011
1 00 PM.-2.00 PM (EST)
Meeting Location: Food and Drug Administration
Building #22, Conference Room #1311
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
Application Number: 105567
Product Name: Ozenoxacin Cream

Indication:



Treatment of impetigo in patients aged 2 years and over.

Sponsor/Applicant Name: Ferrer Internacional S.A.
c/o AAIPharma
Meeting Chair: John Farley, MD. MPH
Meeting Recorder: Fariba Izadi, Pharm.D. RPM

FDA ATTENDEES

Division of Anti-Infective Products

Maria Allende, MD	Clinical Reviewer
David Bostwick	Clinical Reviewer
Celia Cruz, PhD	Product Quality Reviewer
Amy Ellis, PhD	Pharmacology/Toxicology Reviewer
John Farley, MD	Acting Division Director
Mark Gamalo, PhD	Statistics Reviewer
Avery Goodwin, PhD	Clinical Microbiology Reviewer
Fariba Izadi, Pharm.D	Regulatory Health Project Manager
Aryun Kim, Pharm.D	Clinical Pharmacology Reviewer
Katherine A. Laessig, MD	Deputy Director
Frederic Marsik, PhD	Clinical Microbiology Team Leader

Division of Anti-Infective Products (continued)

John Metcalfe, PhD	Product Quality Microbiology Reviewer
Sumathi Nambiar, MD	Deputy Director for Safety
Linda Ng, PhD	Chemistry Team Leader
Wendelyn Schmidt, PhD	Pharmacology/Toxicology Team Leader
Thomas Smith, MD	Clinical Team Leader
Thamban Valappil, PhD	Statistics Team Leader

SPONSOR ATTENDEES

AAIPharma Services:

Christopher Smith	CQE, RAC, Vice President, Corporate Quality Assurance and Regulatory Affairs U.S. Agent for Ferrer Internacional S.A
-------------------	--

Ferrer Internacional S.A.:

Nuria Albareda	BSc, Clinical Research Manager
Domingo Gargallo	PhD, Head of Pharmacology and Safety and Infectious Diseases Manager
Savion Gropper	MD, Head of Clinical Research
Antonio Guglietta	MD, PhD, R&D Director
Gloria Martin	BSc, Head of Documentation and Regulatory Strategy

1.0 BACKGROUND

On April 15, 2011, Ferrer Internacional S.A. c/o AAIPharma submitted an End of Phase 2 meeting request. The briefing package was submitted on May 09, 2011, and contained the questions identified as **Sponsor Question X**. The Division provided preliminary comments to the questions to Ferrer Internacional S.A. c/o AAIPharma, via email on June 8, 2011. These are identified as "**FDA Response to Sponsor Question X**" below. Discussion taking place at the meeting is captured under "**Meeting Discussion**."

2. DISCUSSION

CMC questions (drug product only)

Sponsor Question 1: The Applicant proposes to carry out the proposed Phase 3 clinical studies studies using ozenoxacin 1% cream (b) (4) pilot scale batches. These batches result from an scale-up (b) (4) from previously manufactured (b) (4) clinical batches of ozenoxacin 1% cream with manufacturing being performed at a different manufacturing site (*Ferrer Internacional S.A., Joan Buscallà, 1-9, E-08173 Sant Cugat del Vallès (Barcelona, Spain)*). No significant changes to the manufacturing process are implemented in the manufacturing process of pilot scale batches of ozenoxacin 1% cream compared to previous clinical batches and equivalent equipment, operating principles and procedures are used. Following the principles established in SUPAC-SS CMC 7 guideline

(Guidance for Industry – Nonsterile Semisolid Dosage Forms) and in order to support these changes, prior to the use of these batches in any new clinical trial under this IND, the Applicant plans to obtain results from three months accelerated stability data on at least one ozenoxacin 1% cream pilot scale batch and results from a comparative *in vitro* release rate study of ozenoxacin cream pilot scale batch manufactured in the new manufacturing site vs. prior (b) (4) ozenoxacin cream batch manufactured at the prior site. The applicant believes that the proposed data adequately supports the proposed change and would like to know if FDA agrees with this approach.

FDA Response to Sponsor Question 1: The approach proposed for evaluating the scale up and transfer of pilot clinical batches is adequate if, as stated, “No significant changes to the manufacturing process are implemented in the manufacturing process of pilot scale batches and equivalent equipment, operating principles and procedures are used”.

Please address the following comments:

- a) Please submit information on any *in vitro* method to be used to evaluate (b) (4). As soon as available, submit the *in vitro* test method development and validation reports supporting the selection of the proposed *in vitro* test methodology and release rate.
- b) In future IND updates, please provide numerical results for the degradation product in the batch analysis and stability results. For example, instead of reporting (b) (4) as (b) (4)%, please report the exact reading of the percentage of (b) (4), as detected.
- c) Please provide stability data update to the IND for the clinical lot 001490 ((b) (4) scale, Phase 1), when available.

Meeting Discussion: No discussion was necessary.

Sponsor Question 2: Based on the rationale described in Section 10, it is the Applicant’s opinion that adequate justification for the non-sterility of the product in relation to its intended use is provided. Does the FDA share this opinion?

FDA Response to Sponsor Question 2: Yes, we agree.

Meeting Discussion: No discussion was necessary.

Sponsor Question 3: According to the rationale included in Section 10, the proposed drug product specification does not include homogeneity, particle size distribution or weight loss tests. Does the FDA agree with this approach?

FDA Response to Sponsor Question 3:

Particle Size Distribution:

The stability data provided for the drug substance particle size distribution in the cream, from (b) (4) kg development batches Z02, Z03, B01 1% ozenoxacin and B01 2% ozenoxacin, provide support that the drug substance particle size distribution (b) (4) we recommend including a particle size distribution specification for release and stability of the drug product, in order to address the following during development:

- a) (b) (4)
- (b) (4) Therefore, further development and justification for a proposed drug substance particle size distribution specification, including D10, D50 and D90 is recommended.
- b) Stability of (b) (4) drug substance particle size distribution from relevant scale (Phase 3 or registration batches) held at long term conditions. Currently, no particle size distribution data has been submitted for pilot batches, which may be more representative of the final process.
- c) Impact of (b) (4) drug substance particle size distribution on product performance related to any significant changes to drug substance or drug product process.

At the time of NDA filing, a complete evaluation of the (b) (4) drug substance particle size data from clinical, development, and registration batches can be used to provide a justification for the specification limits and frequency of testing, as appropriate.

Homogeneity:

Homogeneity of the drug product needs to be addressed to ensure consistency of dosing across a batch and consistency of dosing across a single tube (top to bottom). The in-process controls presented to date may provide assurance that the product is homogeneous across the batch, however additional evaluation of preservation of homogeneity upon storage is recommended. At time of NDA submission, please provide homogeneity results on storage from relevant scale batches at appropriate stability testing intervals. When reporting homogeneity results in the future, please include different locations of the container (i.e., top, middle and bottom of the tube) and provide information on the number of tubes tested per batch.

An overall assessment of homogeneity control strategy and stability data will be conducted at the time of NDA review.

Weight Loss:

As development progresses and as part of stability protocol for the NDA registration batches, evaluation of weight loss at relevant storage conditions and different container storage orientations should be conducted. Evaluation of water loss and packaging integrity on storage should be included as part of container closure system development information. Weight loss stability testing should be included at the time of filing, for at least one registration batch held at relevant storage conditions and packaging configurations.

Meeting Discussion: Ferrer asked for further clarification on the Division's comment regarding the evaluation of water loss and storage stability. The Division clarified that water loss is collected from at least one batch through expiry as a one-time study. For storage stability study, tubes are usually stored in inverted or sideways, and upright positions. The worst storage condition is then selected for future annual stability studies.

Ferrer asked if the Franz Cell testing method would be acceptable for evaluating the dissolution method. The Division responded that the proposal appears to be reasonable. However, since such data are reviewed by the biopharmaceutics group, it was recommended that Ferrer submit their dissolution method proposal officially to the IND as soon as feasible for evaluation. Please refer to Response 1 (a).

Non-clinical questions

Sponsor Question 4: Considering that no dermal absorption has been reported in already completed clinical studies and taking into account safety pharmacology and toxicology study reports submitted to IND 105,567 and the currently on-going study P-090768-01 described in Section 10 of this Information Package, is the available safety data of the product adequate and sufficient to adequately support the start of Phase 3 clinical studies in adult and pediatric (> 2 years) population?

FDA Response to Sponsor Question 4: We do not anticipate that any additional nonclinical toxicology data will be needed to support these Phase 3 clinical studies.

Meeting Discussion: No discussion was necessary.

Sponsor Question 5: In the PreIND meeting held with the FDA on September 28th, 2009 the Agency asked the Applicant to perform a 4 week non-clinical dermal toxicology study on intact and wounded skin. In order to fulfill this requirement the Applicant has conducted study P-090768-01. The experimental part of this study has already been completed and the final report is

currently under preparation (a copy of the protocol is included in Appendix XI and a summary of the preliminary results of this study are enclosed in Section 10). Does the Agency consider this study appropriate to fulfill the PreIND meeting requirement above mentioned?

FDA Response to Sponsor Question 5: The protocol for this study appears appropriate. Pending review of the final report for this study, it appears that the Division's request has been fulfilled.

Meeting Discussion: No discussion was necessary.

Sponsor Question 6: In the PreIND meeting held with the FDA on September 28th, 2009 the Agency asked the Applicant to provide additional microbiological data and made several recommendations on the microbiological development of ozenoxacin. Following the Agency advice, the Applicant has already completed several microbiological studies to address these requirements (reports of these studies have been already submitted to IND 105,567 and a Pharmacodynamics Update is enclosed as Appendix I). The Applicant is also currently performing or planning to perform several additional studies (details on these studies are described under Appendices II, III, IV and V). Does the Agency consider that the already available results of the *in vitro/in vivo* non-clinical studies completed by the on-going and planned studies adequately and sufficiently characterize the antimicrobial effect of ozenoxacin?

FDA Response to Sponsor Question 6: Yes, the Agency agrees that the *in vitro* and *in vivo* non-clinical studies completed and planned adequately characterize the antimicrobial effect of ozenoxacin.

Meeting Discussion: No discussion was necessary.

Sponsor Question 7: In order to monitor the worldwide susceptibility of ozenoxacin the Applicant has conducted study P-090788-01 (a copy of the protocol and study report are enclosed as Appendices II and III) and plans to complete study RYC-OZE-3 (outline of the protocol described in Appendix V) before NDA submission. Does the agency consider this plan adequate for the registration of ozenoxacin cream?

FDA Response to Sponsor Question 7: You have indicated that your aim is to establish QC ranges as indicated in the CLSI M23-A3 document and have made reference to the completion of this study (Study Reference # RYC-OZE-3) in 2012-2013. Quality control data is necessary for the accuracy of ozenoxacin susceptibility testing. The quality control organisms are used to check that ozenoxacin concentrations were made properly and that the antibiotic in the test media is correct. According to our guidance, we recommend that QC parameters for *in vitro* antibacterial susceptibility tests should be established before determining the activity of the antibacterial drug product against microorganisms to

ensure the generation of precise, accurate, and reproducible results. These QC parameters should be determined before Phase 2 clinical studies. Since you have completed your Phase 2, we strongly recommend that you establish QC parameters before Phase 3.

Meeting Discussion: Ferrer stated that they have completed and established QC parameters and the report would be submitted shortly. The Division stated that the report would be reviewed and feedback would be provided. The Division noted that using CLSI-M23 should be sufficient for establishing QC parameters.

The Division stated that the QC parameters should be established prior to initiating Phase 3. The Division confirmed that the protocol for collecting the data with respect to worldwide susceptibility was acceptable.

Additional comments:

- a) You stated in the clinical study protocol that in the case of bullous lesions the sample should be collected preferably by aseptic needle aspiration or alternatively by swabbing the bullous exudates. The Agency recognizes that tissue or fluid is superior to swab specimens; however, if swabs are used it may be worthwhile to collect two swabs, one for culture and one for Gram stain. Swabs of purulence originating from beneath the dermis are appropriate.

Meeting Discussion: Ferrer asked if it was acceptable to collect two swabs instead of collecting tissue or fluid samples since there were concerns from ethics committees and parents regarding needle aspiration. The Division stated that specimens from patients with bullous impetigo should be collected from intact bullae by needle aspiration. The Division reminded the sponsor that this is a painless procedure and should not raise any concerns. The Division stated that it is difficult to get reliable swab cultures from ruptured bullous lesions due to possible contamination. The Division further noted that sampling with swabs, using the method described in the draft protocol, is considered acceptable for crusted impetigo.

- b) In the clinical study all *S. aureus* isolates should be tested for the presence of *pvl* gene. The Agency is interested in the clinical outcome of isolates that test positive (or negative) for *pvl*.

Meeting Discussion: Ferrer asked about the logic behind the Division's interest in the clinical outcome of isolates that have the *pvl* gene. The Division explained that there seems to be a correlation between *pvl* and disease activity. In the past, the Division has asked the sponsors to test for the presence of the *pvl* gene to better understand the relationship between the presence of *pvl* and disease severity.

- c) You have demonstrated the importance of pH on MIC determination of ozenoxacin; and in one study you also showed that high inoculum ($>10^7$ CFU/mL) resulted in an 8-fold increase in MIC of your study drug. Did you

measure the pH of the medium following the addition of the high inoculum cell suspension; do you think the high inoculum may have caused the change in pH and contributed to the increase in MIC?

Clinical questions

Sponsor Question 8: Is the design of the proposed Phase 3 clinical study **P-110880-01** (draft protocol included in Appendix VI) considered adequate specially taking into account the clinical and microbiology assessment, the microbiology sampling method and the inclusion/exclusion criteria?

FDA Response to Sponsor Question 8: Please note the following comments:

- a) The definition of clinical success at the end of treatment should require that the SIRS score be 0 for exudate/pus, crusting, tissue warmth and pain and no more than 1 each for erythema/inflammation, tissue edema and itching. All other outcomes with the exception of “unable to determine” should be classified as failures. The definition of clinical success at follow-up should require that SIRS scores be 0 for all evaluated signs/symptoms. Both definitions presume that no additional antimicrobial therapy is required outside the test preparations assigned during the 5 day treatment period.
- b) Microbiological samples should be obtained from all test subjects.
- c) The inclusion/exclusion criteria are satisfactory, with the exception that patients should have a pus/exudate SIRS score of at least 1 to enter the study.
- d) An additional secondary efficacy variable which addresses wound size (or area infected) should be added to the protocol.
- e) Primary efficacy analysis should be performed on the ITT population, i.e., all randomized patients regardless of whether the subject is given the medication. This applies to all three studies.

Meeting Discussion: The Division confirmed that the primary endpoint evaluation is based on the results of the sign and symptom (SIRS) score.

Sponsor Question 9: Is the design of the proposed Phase 3 clinical study **P-110881-01** (draft protocol included in Appendix VII) considered adequate specially taking into account the clinical and microbiology assessment, the microbiology sampling method and the inclusion/exclusion criteria?

FDA Response to Question 9: The comments above for Study P-110880-01 also apply to this study.

We recommend that the randomization allocation ratio of 1:1 be used in this study.

Meeting Discussion: No discussion was necessary.

Sponsor Question 10: [REDACTED] (b) (4)
[REDACTED] considered adequate specially taking into account the clinical and microbiology assessment, the microbiology sampling method and the inclusion/exclusion criteria?

FDA Response to Sponsor Question 10: Please note the following comments:

[REDACTED] (b) (4)

Meeting Discussion: No discussion was necessary.

Sponsor Question 11: In the PreIND meeting held with the FDA on September 28th, 2009 the Agency asked the Applicant to collect data on the pharmacokinetics (absorption) profile of the to be marketed formulations in patients with the indicated [REDACTED] (b) (4) impetigo [REDACTED] (b) (4) prior the approval of this product. Is the design of the following proposed studies considered appropriate to fulfill this requirement?

- **Study P-100797-01:** PK impetigo adults and children (draft protocol included in Appendix IX).

[REDACTED] (b) (4)

FDA Response to Question 11: There is no clinical comment concerning Study P-110797-01. [REDACTED] (b) (4). We will use Study P-100797-01 to determine whether studies in QT prolongation will be required.

Please see also the comments concerning the pediatric plan below.

Meeting Discussion: No discussion was necessary.

Sponsor Question 12: Are the already performed and on-going clinical studies together with the planned clinical studies in patients with impetigo (P-110880-01, P-110881-01, P-100797-01) presented in the clinical development summary included in the Background Section of this Information package sufficient to support the safety and efficacy of the product for the impetigo indication?

FDA Response to Sponsor Question 12: If the revisions noted above are implemented, DAIP agrees that the proposed studies, if successful, are adequate to support the safety and efficacy of this product in impetigo.

Meeting Discussion: No discussion was necessary.

Sponsor Question 13:

(b) (4)

(b) (4)

FDA Response to Sponsor Question 13:

(b) (4)

(b) (4)

Meeting Discussion: No discussion was necessary.

Pediatric Plan question

Sponsor Question 14: Does the FDA agree with the proposed Pediatric Plan for the impetigo indication including waiver (b) (4) requests/proposals included in Appendix XII?

FDA Response to Sponsor Question 14:

(b) (4)

(b) (4)

(b) (4)

We concur with your plan to request for a partial waiver in children aged 0-2 months for the impetigo indication. In your NDA submission, you should provide justification to support your request for the partial waiver.

Meeting Discussion:

(b) (4)

(b) (4)

(b) (4)



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

/s/

JANE A DEAN
07/07/2011

JOHN J FARLEY
07/07/2011

LATE-CYCLE COMMUNICATION
DOCUMENTS



NDA 208945

LATE-CYCLE MEETING MINUTES

Ferrer Internacional S.A.
c/o Prosoft Clinical
Attention: Robert W. Babilon, MS, MBA
Vice President, Regulatory Affairs and Quality Assurance
996 Old Eagle School Road, Suite 1106
Wayne, PA 19087

Dear Mr. Babilon:

Please refer to your New Drug Application (NDA) dated June 23, 2016, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Ozenoxacin Cream, 1%.

We also refer to the Late-Cycle Meeting (LCM) between representatives of your firm and the FDA on March 24, 2017.

A copy of the official minutes of the LCM is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Eva Zuffova, PhD, MS, Regulatory Health Project Manager at (301) 796-0697.

Sincerely,

{See appended electronic signature page}

Thomas Smith, MD
Cross Discipline Team Leader
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure:
Late Cycle Meeting Minutes



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF LATE-CYCLE MEETING MINUTES

Meeting Date and Time: March 24, 2017; 9:00AM-10:00AM
Meeting Location: Teleconference
Application Number: NDA 208945
Product Name: Ozenoxacin Cream, 1%
Applicant Name: Ferrer Internacional, S.A.

Meeting Chair: Thomas Smith, MD
Meeting Recorder: Eva Zuffova, PhD

FDA ATTENDEES

Office of Antimicrobial Products

John Farley, MD, MPH Deputy Director

Division of Anti-Infective Products

Abimbola Adebowale, PhD	Associate Director of Labeling
David Bostwick	Clinical Reviewer
Jane Dean, RN, MSN	Regulatory Health Project Manager
Avery Goodwin, PhD	Clinical Microbiology Reviewer
Dmitri Iarikov, MD, PhD	Deputy Director (Acting)
Seong Jang, PhD	Clinical Pharmacology Team Leader
Dorota Matecka, PhD	Chemistry, Manufacturing and Controls (CMC) Lead
Sumathi Nambiar, MD, MPH	Director
Terry Miller, PhD	Pharmacology/Toxicology Team Leader
Nicholas Rister, MD	Clinical Reviewer
Thomas Smith, MD	Cross Discipline Team Leader
Xiaohui Wei, PhD	Clinical Pharmacology Reviewer
Joseph Toerner, MD, MPH	Deputy Director for Safety
Eva Zuffova, PhD, MS	Regulatory Health Project Manager

Division of Biometrics IV

Karen Higgins, ScD	Statistical Team Leader
Christopher Kadoorie, PhD	Statistical Reviewer

Office of Product Quality

David Anderson, PhD	Facilities Reviewer
Kaushalkumar Dave, PhD	Biopharmaceutics Reviewer
Alifiya Ghadiali, PhD	Product Quality Microbiology Reviewer
Derek Smith, PhD	Branch Chief (Acting)

Office of Scientific Investigations

Sharon Gershon, PharmD

Good Clinical Practice Reviewer

Office of Surveillance and Epidemiology

Till Olickal, PhD, PharmD

Risk Management Analyst

APPLICANT ATTENDEES

Finished Product, Sponsor (FERRER INTERNACIONAL, S.A.)

Fabiana D'Aniello	Project Director
Pablo Martín	Head of Pharmaceutical Development
José Ignacio Escamilla	Formulation Development Scientist
Sergio González,	Manager Analytical Development
Marta Fernández	Analytical Development
Núria Albareda	Clinical Development
Ilonka Zsolt	Medical Department
Cristina Casado	Regulatory Affairs
Laura Moya	Regulatory Affairs
Silvia Martín	Corporate Director, Regulatory Affairs & Compliance

API

(b) (4)

(b) (4)

Regulatory Affairs
Quality Assurance

Medimetriks

Noah Rosenberg
Sandra Roth
Donna Heren

Chief Medical Officer
Director, Clinical Development
Vice President (VP), Regulatory Affairs and Quality Assurance
Associate, Regulatory Affairs and Quality Assurance

Drug Product

Nadya Lawrence
(b) (4), PhD

Senior VP, Technical Services, Teligent

Director, Microbiological Services, (b) (4)

(b) (4)

VP, Quality Assurance & Regulatory Affairs, (b) (4)

(b) (4)

Prosoft Clinical

Robert Babilon

US Liaison

1.0 BACKGROUND

NDA 208945 was submitted on June 23, 2016 for ozenoxacin cream, 1%.

Proposed indication(s): Topical treatment of impetigo in adults, adolescents, children (b) (4)
(b) (4) 2 months and older

PDUFA goal date: June 22, 2017

FDA issued a Background Package in preparation for this meeting on March 10, 2017.

2.0 DISCUSSION

1. Introductory Comments – Thomas Smith
Welcome, Introductions, Objectives of the meeting
 2. Discussion of Substantive Review Issues
Each issue was introduced by FDA and followed by a discussion.
- Product Quality

The FDA stated that the Product Quality review is pending and acknowledged the Applicant's responses to a number of information requests previously conveyed to the Applicant. The FDA stated that there are still several pending product quality issues, such as status of manufacturing facilities, equipment compatibility and holding times in the manufacturing process, and product quality microbiology controls, which must be resolved.

Discussion-2a: The Division provided the following information on inspection of the (b) (4) manufacturing facility.

- During a recent inspection of the (b) (4) manufacturing facility for this NDA, our field investigator observed objectionable conditions at the facility and conveyed that information to the representative of the facility at the close of the inspection. Satisfactory resolution of the observations is required before this application may be approved.

Ferrer stated that concerns cited in the warning letter have been addressed, and corrective actions implemented. They will inform the FDA about re-inspection, and anticipate a positive outcome. The FDA noted that the Applicant must contact the Office of Compliance, through the contact person noted in the Warning Letter.

Discussion-2b: The Division provided the following information on issues related to the equipment compatibility and proposed holding times in the manufacturing process, and product quality microbiology controls.

- We have identified issues related to the equipment compatibility and proposed holding times in the manufacturing process, and product quality microbiology controls, which need to be addressed (refer to detailed comments conveyed in the Information Request (IR) letters dated February 2, and March 7, 2017).

Ferrer stated that results of the proposed

(b) (4)

(b) (4)

(b) (4)

(b) (4) A

The FDA noted the challenges in the microbial growth assay and agreed that a response with a rationale for the approach taken should be submitted for review in the response to the IR.

3. Additional Applicant Data

Discussion: No discussion was needed.

4. Information Requests

IR letters issued February 2, and March 7, 2017.

Responses are due to the FDA on March 27, 2017.

Discussion: No discussion was needed.

5. Major Labeling Issues - 5 minutes

Discussion: No discussion was needed.

6. Review Plans

Action/PDUFA Goal Date under the program: June 22, 2017

Discussion: No discussion was needed.

7. Wrap-up and Action Items

This application has not yet been fully reviewed by the signatory authority, division director, and Cross-Discipline Team Leader (CDTL) and therefore, this meeting did not address the final regulatory decision for the application.

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

/s/

SUMATHI NAMBIAR

04/20/2017

signed on behalf of Dr. Thomas Smith.