CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205572Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 205572 SUPPL # HFD #

Trade Name Moxifloxacin 400mg/250ml

Generic Name

Applicant Name FK

Approval Date, If Known 04-03-15

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

505 (b)(2)

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.

This submission is for a dosage form that is currently approved. It did not require clinical data or bioequivalence studies. The Sponsor had requested a waiver of bioequivalence studies.

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:

N/A

d) Did the applicant request exclusivity?

YES ☐ NO ☒

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

N/A

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#	21277	Avelox IV
NDA#	21085	Avelox Tablet
NDA#	21598	Vigamox ophthalmic solution
NDA	22428	Moxeza ophthalmic solution
ANDA	77437	Moxifloxacin HCL tablets

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 ☐ NO ☐

Investigation #2 YES ☐ NO ☐

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 ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !
!
IND # YES ☐ ! NO ☐
! Explain:

Investigation #2 !
!
IND # YES ☐ ! NO ☐
! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	!
	!
YES ☐	! NO ☐
Explain:	! Explain:

Investigation #2	!
	!
YES ☐	! NO ☐
Explain:	! 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: Fariba Izadi, PharmD
Title: Regulatory Health Project Manager
Date: 03-26-15

Name of Office/Division Director signing form: Sumathi Nambiar, MD. MPH
Title: Division Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

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

/s/

FARIBA IZADI
04/03/2015

SUMATHI NAMBIAR
04/03/2015

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION[1]

NDA # 205572 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: *(an action package is not required for SE8 or SE9 supplements)*
Proprietary Name: Established/Proper Name: Moxifloxacin Dosage Form: Sterile Injectable Solution		Applicant: Fresenius Kabi USA, LLC Agent for Applicant (if applicable):
RPM: Fariba Izadi		Division: Anti-Infective Products

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 draft[2] 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: 03-20-15

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.

❖ Actions	
• Proposed action • User Fee Goal Date is April 03, 2015	☒ AP ☐ TA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☐ None Complete Response 04-04-14
❖ 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 _____	☐ Received
❖ 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. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

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

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

NDAs: Subpart H
☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)
Subpart I
☐ Approval based on animal studies

BLAs: Subpart E
☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)
Subpart H
☐ 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

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)*	☐ Yes ☐ No
❖ 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)? • If so, specify the type	☒ No ☐ Yes
❖ 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 on FDA 3542 a ☒ 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) 04-03-15 Approval 04-04-14 Complete Response
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)*	N/A
❖ Labeling reviews *(indicate dates of reviews)*	RPM: ☒ 04-02-14 DMEPA: ☒ 03-17-15 02-20-15, 12-17-13 DMPP/PLT (DRISK): ☒ 03-19-15 OPDP: ☒ 03-12-15 02-19-14 SEALD: ☒ None CSS: ☒ None Other: ☒ None
Administrative / Regulatory Documents	
❖ RPM Filing Review[4]/Memo of Filing Meeting *(indicate date of each review)* ❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	03-28-14 03-05-15 03-07-14
❖ NDAs only: Exclusivity Summary *(signed by Division Director)*	☒ Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	

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

• Applicant is on the AIP	☐ Yes ☒ No
• 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:	This application does not contain new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration.
❖ 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, etc.) *(do not include previous action letters, as these are located elsewhere in package)*	Included
❖ 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)	Included
❖ Minutes of Meetings	
• If not the first review cycle, any end-of-review meeting *(indicate date of mtg)*	no mtg
• Pre-NDA/BLA meeting *(indicate date of mtg)*	N/A
• EOP2 meeting *(indicate date of mtg)*	N/A
• Mid-cycle Communication *(indicate date of mtg)*	N/A
• Late-cycle Meeting *(indicate date of mtg)*	N/A
• Other milestone meetings (e.g., EOP2a, CMC pilots) *(indicate dates of mtgs)*	N/A
❖ Advisory Committee Meeting(s)	No AC meeting
• Date(s) of Meeting(s)	N/A
Decisional and Summary Memos	
❖ Office Director Decisional Memo *(indicate date for each review)*	☒ None
Division Director Summary Review *(indicate date for each review)*	04-03-15 & 04-04-14
Cross-Discipline Team Leader Review *(indicate date for each review)*	03-19-14 (First Cycle)
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)*	03-07-15 02-05-14-first cycle
• 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)*	No clinical studies needed.
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers *(indicate date of each review)*	☒ 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 ☒ None
❖ OSI Clinical Inspection Review Summary(ies) *(include copies of OSI letters to investigators)*	☒ None requested
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)*	☒ 01-28-15 02-15-14-first cycle
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)*	☒ 03-17-15 03-19-14-first cycle
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)*	☒ 03-11-15 02-04-14 first cycle
❖ OSI Clinical Pharmacology Inspection Review Summary *(include copies of OSI letters)*	☒ None requested
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)*	☒ None 03-09-15 02-14-14-first cycle
❖ 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 Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary *(include copies of OSI letters)*	☒ None requested

Product Quality ☐ None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) *(indicate date for each review)*	☒ No separate review
• Branch Chief/Team Leader Review(s) *(indicate date for each review)*	☒ No separate review
• Product quality review(s) including ONDQA biopharmaceutics reviews *(indicate date for each review)*	☒ 02-13-14 Biopharm 03-12-15 01-27-14-first cycle
❖ Microbiology Reviews ☒ NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) *(indicate date of each review)* ☐ BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) *(indicate date of each review)*	02-10-14
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer *(indicate date of each review)*	☒ Biopharm 03-12-15 01-27-14
❖ 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)*	Acceptable on 02/07/2014
☐ Review & FONSI *(indicate date of review)*	
☐ Review & Environmental Impact Statement *(indicate date of each review)*	
❖ Facilities Review/Inspection	
☐ NDAs: Facilities inspections (include EER printout or EER Summary Report only; do NOT include EER Detailed Report; date completed must be within **2 years** of action date) *(only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites[5])*	Date completed: 04-02-15 ☒ Acceptable ☐ Withhold recommendation ☐ Not applicable
☐ BLAs: TB-EER (date of most recent TB-EER must be within **30 days** of action date) *(original and supplemental BLAs)*	Date completed: 04-02-15 ☒ Acceptable ☐ Withhold recommendation
❖ NDAs: Methods Validation *(check box only, do not include documents)*	☐ Completed ☐ Requested ☐ Not yet requested ☒ Not needed (per review)

[5] i.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

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 *(Notify CDER OND IO)*
• Finalize 505(b)(2) assessment	☒ Done
❖ For Breakthrough Therapy(BT) Designated drugs: • Notify the CDER BT Program Manager	N/A *(Send email to CDER OND IO)*
❖ For products that need to be added to the flush list (generally opioids): • Notify the Division of Online Communications, Office of Communications	N/A
❖ 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	N/A
❖ Ensure that proprietary name, if any, and established name are listed in the *Application Product Names* section of DARRTS, and that the proprietary name is identified as the "preferred" name	N/A
❖ Ensure Pediatric Record is accurate	☐ Done-exempt
❖ Send approval email within one business day to CDER-APPROVALS	☒ Done

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

/s/

FARIBA IZADI
04/03/2015

From: Izadi, Fariba
Sent: 4/1/2015 3:31:32 PM
To: 'Andrea.Redd@fresenius-kabi.com'
Subject: NDA 205572-comments and information requests
Importance: High

Dear Andrea,

We are reviewing your NDA submission dated October 04, 2015 and have the following comments from our Product Quality team.

You have proposed a (b) (4) month expiration period based on the stability data submitted on three pilot batches at 6 months accelerated (40 °C/≤ 25 % RH) and 24 months long-term (25 °C/40 % RH). The migration studies performed on same batches 12FCU92, 12FCU93, and 12FCU92 were updated and provide the concentration up to 24 months for the identified leachables. Based on the evaluation of the presented stability and migration data the recommended expiration period is for (b) (4) months.

Best regards

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@fda.hhs.gov

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

/s/

FARIBA IZADI
04/02/2015

From: Izadi, Fariba
Sent: 3/18/2015 2:50:38 PM
To: 'Andrea.Redd@fresenius-kabi.com'
bject: NDA 205572-moxifloxacin-Response to information request and additional comments
Importance: High

Dear Andrea,

We have reviewed your responses to our information requests sent via email on March 06, 2015 and have the following comments from the Division of Medication Error Prevention and Analysis (DMEPA) regarding the bag label and overwrap labeling.

1. Remove the second strength presentation (400 mg) as this additional statement is an incomplete strength statement and would mislabel the product since the appropriate strength should be expressed as the total strength per total volume in accordance with
the USP General Chapter <1> INJECTIONS.

2. We recommend that the prominence of the storage statement be increased by capitalizing each word as follows: "DO NOT REFRIGERATE – PRODUCT PRECIPITATES UPON REFRIGERATION", on both the bag label and overwrap labeling be implemented.

In addition, we have the following comment from our Product Quality Team.

3. Remove the "(as hydrochloride)" as found in several places on the labels.
   1) The "* " equivalent statement needs to be changed for accuracy perhaps as:
      *a) * 400mg moxifloxacin is equivalent to XXX mg of moxifloxacin hydrochloride*
      b) or perhaps eliminate/remove the "*" and statement all together, the strength is already expressed in terms free base and the HCl information will be in PI.

Best regards

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@fda.hhs.gov

From: Izadi, Fariba
Sent: 3/2/2015 4:23:17 PM
To: 'Andrea.Redd@fresenius-kabi.com'
Subject: NDA 205572-moxifloxacin injection-information request
Importance: High

Dear Ms. Redd,

We are reviewing your application dated October 03, 2014 for NDA 205572 (moxifloxacin) and have the following comments and information requests from our team regarding the Bag label and Overwrap Labeling.

1. Please ensure that the entire name, which includes the dosage form, appears in a single font size.

2. Increase the prominence of important storage information by capitalizing the statement "DO NOT REFRIGERATE – PRODUCT RECIPITATES UPON REFRIGERATION'.

3. Remove (b) (4) as it may pose dosing confusion and be misinterpreted as the total volume of the bag.

Best regards

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@fda.hhs.gov

Please confirm receipt of this email

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/s/

FARIBA IZADI
03/02/2015

From: Izadi, Fariba
Sent: 1/12/2015 1:57:24 PM
To: 'Andrea.Redd@fresenius-Kabi.com'
Subject: NDA 205572-Moxifloxacin 400 mg/ 250 ml-Resubmission-Information request
Signed By:

Importance: High

Dear Ms. Redd,

We are reviewing your application dated October 03, 2014 for NDA 205572 (moxifloxacin) and have the following comments and information requests from our biopharmaceutics team.

You have not provided adequate supportive information demonstrating that the physiological disposition of your proposed and listed drug products are similar despite the differences in the inactive ingredients. To support the approval of the biowaiver, submit strong justification and evidence that with the inclusion of sodium acetate trihydrate and disodium sulfate, the physiological disposition (i.e. metabolism and excretion) of your proposed drug product is not different than that of the listed drug product upon administration. You may include literature references to support your justification.

We request this information by **COB February 09, 2015.**

Best regards

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@fda.hhs.gov

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/s/

FARIBA IZADI
01/12/2015

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205572

ACKNOWLEDGE –
CLASS 2 RESUBMISSION

Fresenius Kabi USA, LLC
Attention: Nicole Cage
Senior Regulatory Specialist
Three Corporate Drive
Lake Zurich, IL 60047

Dear Ms. Cage:

We acknowledge receipt on October 03, 2014, of your October 03, 2014, resubmission to your new drug application submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Moxifloxacin Injection 400 mg/250 mL.

We consider this a complete, class 2 response to our April 04, 2014 action letter. Therefore, the user fee goal date is April 03, 2015.

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

Sincerely,

{See appended electronic signature page}

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

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/s/

FRANCES V LESANE
10/21/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205572

ACKNOWLEDGE INCOMPLETE RESPONSE

Fresenius Kabi USA, LLC
Attention: Nicole Cage
Senior Regulatory Specialist
Three Corporate Drive
Lake Zurich, IL, 60047

Dear Ms. Cage:

We acknowledge receipt on August 29, 2014, of your August 29, 2014, submission to your New Drug Application (NDA) for Moxifloxacin Injection 400 mg/250 ml.

We do not consider this a complete response to our April 04, 2014 action letter. Therefore, we will not start the review clock until we receive a complete response. The following deficiency from our action letter still needs to be addressed:

A DMF deficiency letter was sent to the DMF holder on June 24, 2013. Please follow up with the DMF holder to ensure that the deficiencies have been addressed.

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

Sincerely,

{See appended electronic signature page}

Sumathi Nambiar, MD, MPH
Director
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

SUMATHI NAMBIAR
09/12/2014

Izadi, Fariba

From: Izadi, Fariba
Sent: Friday, April 04, 2014 2:20 PM
To: 'Nicole.Cage@fresenius-kabi.com'
Subject: NDA 205572-moxifloxacin- Comments and Information requests

Importance: High

Dear Ms. Cage,

We have the following comments and Information requests regarding your submission dated June 06, 2013 for NDA 205572 (moxifloxacin 400 mg/250 ml).

1. Revise the storage statement from (b) (4) to the USP controlled room storage statement "Store at 20-25°C (68-77°F) [see USP Controlled Room Temperature (b) (4)].

2. Ensure that the presentation of the established name and statement of infusion time are consistent with the finalized insert labeling.

3. Ensure that the product name and strength statements are the most prominent information on the label by significantly increasing their size. Also ensure that the entire name, which includes the dosage form, appears in a single font size. The NDC number competes for prominence with the name and strength statement. Decrease the size of the NDC number and relocate it higher on the label, away from the name.

4. Increase the prominence of important storage information by increasing the size and bolding the statement "DO NOT REFRIGERATE – PRODUCT PRECIPITATES UPON REFRIGERATION'.

5. To reduce clutter, ensure there is adequate empty space below the infusion time statement.

6. To improve readability, revise the text under the infusion time statement, from all capital letters to title case (as in the overwrap labeling and except for the "DO NOT REFRIGERATE PRODUCT PRECIPITATES UPON REFRIGERATION" statement).

Please do not hesitate to contact me if you need further assistance.

Best regards

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@fda.hhs.gov

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/s/

FARIBA IZADI
04/04/2014

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy Initiatives
Division of Medical Policy Programs

REVIEW DEFERRAL MEMORANDUM

Date:	February 10, 2014
To:	Sumathi Nambiar, MD Acting Director **Division of Anti-Infective Products (DAIP)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Melissa Hulett, MSBA, BSN, RN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Robin Duer, MBA, BSN, RN Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)**
Subject:	Review Deferred: Medication Guide (MG)
Drug Name (established name):	moxifloxacin hydrochloride injection
Dosage Form and Route:	solution for IV use
Application Type/Number:	NDA 205572
Applicant:	Fresenius Kabi USA, LLC

1 INTRODUCTION

On June 6, 2013, Fresenius Kabi USA, LLC submitted for the Agency's review a New Drug Application (NDA) for moxifloxacin hydrochloride injection, solution for IV use. Moxifloxacin hydrochloride injection is a fluoroquinolone antibacterial indicated for treating infections in adults ≥ 18 years of age caused by designated, susceptible bacteria. The reference listed drug (RLD) for moxifloxacin hydrochloride injection is Avelox (moxifloxacin) hydrochloride injection, solution for IV use.

On October 1, 2013, the Division of Anti-Infective Products (DAIP) requested that the Division of Medical Policy Programs (DMPP) review the Applicant's proposed Medication Guide (MG) for for moxifloxacin hydrochloride injection.

This memorandum documents the DMPP review deferral of the Applicant's proposed MG for moxifloxacin hydrochloride injection.

2 CONCLUSIONS

Due to outstanding chemistry deficiencies, DAIP plans to issue a Complete Response (CR) letter. Therefore, DMPP defers comment on the Applicant's patient labeling at this time. A final review will be performed after the Applicant submits a complete response to the Complete Response (CR) letter. Please send us a new consult request at such time.

Please notify us if you have any questions.

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/s/

ROBIN E DUER
02/10/2014

MELISSA I HULETT
02/10/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205572

INFORMATION REQUEST

Fresenius Kabi USA, LLC
Attention: Nicole Cage
Senior Regulatory Specialist
Three Corporate Drive
Lake Zurich, IL, 60047

Dear Ms. Cage:

Please refer to your New Drug Application (NDA) dated June 06, 2013, received June 07, 2013 submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Moxifloxacin Injection 400 mg/250 ml.

We are reviewing the Non-Clinical and Product Quality sections of your submission and have the following comments and information requests. We request a prompt written response preferably by December 03, 2013, in order to continue our evaluation of your NDA.

Non-clinical

Provide any additional toxicity information for each of these three identified leachables (b) (4) and the "related" compounds from nonclinical studies you may have conducted, from studies described in published literature, or from public toxicity databases. Also, include a more detailed rationale for your selection of "related" compounds used to determine the PDE for each of the identified leachables for which no toxicity information is available.

Product Quality

1. With respect to moxifloxacin injection in 300 mL Free*flex* Bags, you have only provided leachable data on one batch at 6 months. The amount of data provided is insufficient to justify the exclusion of leachable testing in the drug product specification. Establish tentative acceptance criteria for four leachables, (b) (4) in the drug product specification and provide justification for the proposed acceptance criteria. Include monitoring leachable levels on stability until end of shelf-life for the 3 ongoing registration stability batches, and for each annual batch as part of post-approval stability protocol. If data from a sufficient number of commercial scale batches show negligible levels of leachables or data is generated to provide accurate PDE for each leachable as requested in the DMF deficiency letter, you may propose to eliminate the leachable test. It will be valuable to test

the leachable levels in the 3 registration stability batches and the batch for which the 6 month leachable data was provided, and report the data to the NDA during this review cycle.

2. The conditions used for extraction testing of 300 mL Free*flex* bags do not appear to have been exhaustive to establish appropriate acceptance criteria for leachables in the container closure raw material. Specifically, you did not conduct studies in alcohol and at pH 2 solution, and studies were done only over 1 hour. Using methods that meet or exceed USP, determine total extractables for drug product contact materials [redacted] (b) (4) in a one-time extraction study in water for injections (WFI), pH 2, pH 8.0, and alcohol. Reflux in the extraction media at hourly intervals until the extractables are exhausted from material. Calculate new safety factors for each using these values. Please also report these data to your type III DMF [redacted] (b) (4).

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

Sincerely,

{See appended electronic signature page}

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

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/s/

SUMATHI NAMBIAR
10/22/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205572

FILING COMMUNICATION –
NO FILING REVIEW ISSUES IDENTIFIED

Fresenius Kabi USA, LLC
Attention: Nicole Cage
Senior Regulatory Specialist
Three Corporate Drive
Lake Zurich, IL, 60047

Dear Ms. Cage:

Please refer to your New Drug Application (NDA) dated June 06, 2013, received June 07, 2013 submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Moxifloxacin Injection 400 mg/250 ml.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard** and the user fee goal date is April 07, 2014.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by March 11, 2014. In addition, the planned date for our internal mid-cycle review meeting is November 06, 2013. We are not currently planning to hold an advisory committee meeting to discuss this application.

At this time, we are notifying you that, we have not identified any potential review issues. Please note that our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

We request that you submit the following information:

1. Provide data/justification (e.g. comparison of API solubility, drug product osmolality, and drug product pH) demonstrating that the human physiological disposition (i.e., metabolism and excretion) of the proposed product and the reference product is similar, despite the formulation differences between these drug products.

2. The draft package insert and container labels submitted in Section 1.14.1 describe the (b) (4). In addition, the various sections of the labeling list (b) (4) as drug product components. However, the proposed drug product formulation provided in section 3.2.P.1 of Module 3 does not include these ingredients. Please resolve this discrepancy and submit a correct version of the draft container labels and package insert for the drug product.

Please respond only to the above requests as soon as possible. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

PROMOTIONAL MATERIAL

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI) Medication Guide. Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Do not submit launch materials until you have received our proposed revisions to the package insert (PI), Medication Guide, and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm. If you have any questions, call OPDP at 301-796-1200.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

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

Sincerely,

{See appended electronic signature page}

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

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/s/

SUMATHI NAMBIAR
08/15/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205572

NDA ACKNOWLEDGMENT

Fresenius Kabi USA, LLC
Attention: Ms. Nicole Cage
Senior regulatory Specialist
Three Corporate Drive
Lake Zurich, IL 60047

Dear Ms. Cage:

We have received your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Moxifloxacin 400 mg/250 mL

Date of Application: June 06, 2013

Date of Receipt: June 07, 2013

Our Reference Number: NDA 205572

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 06, 2013 in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

The NDA number provided above should be cited 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 Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm.

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to SecureEmail@fda.hhs.gov. Please note that secure email may not be used for formal regulatory submissions to applications.

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

Sincerely,

{See appended electronic signature page}

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

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/s/

FRANCES V LESANE
06/27/2013