APPLICATION NUMBER:

208610Orig1s000
208611Orig1s000

OTHER REVIEW(S)
**PMR/PMC Development Template**

This template should be completed by the PMR/PMC Development Coordinator and included for each PMR/PMC in the Action Package.

<table>
<thead>
<tr>
<th>NDA/BLA #</th>
<th>NDA 208610 &amp; NDA 208611</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product Name:</td>
<td>Baxdela (delafloxacin) 450 mg Tablets (NDA 208610) and Baxdela (delafloxacin) 300 mg Injection (NDA 208611).</td>
</tr>
</tbody>
</table>

**PMR/PMC Description:** 3220-1 Conduct US surveillance studies for five years from the date of marketing BAXDELA to determine if resistance to delafloxacin has developed in those organisms specific to the indication in the label for ABSSSI.

**PMR/PMC Schedule Milestones:**
- Final Protocol Submission: 09/30/2017
- Study/Trial Completion: 09/30/2022
- Final Report Submission: 12/31/2022
- Other:
  - First interim report: 07/31/2018
  - Second interim report: 07/31/2019
  - Third interim report: 07/31/2020
  - Fourth interim report: 07/31/2021
  - Fifth interim report: 07/31/2022

1. During application review, explain why this issue is appropriate for a PMR/PMC instead of a pre-approval requirement. Check type below and describe.

<table>
<thead>
<tr>
<th>Option</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
<td>Unmet need</td>
</tr>
<tr>
<td>☐</td>
<td>Life-threatening condition</td>
</tr>
<tr>
<td>✗</td>
<td>Long-term data needed</td>
</tr>
<tr>
<td>✗</td>
<td>Only feasible to conduct post-approval</td>
</tr>
<tr>
<td>☐</td>
<td>Prior clinical experience indicates safety</td>
</tr>
<tr>
<td>☐</td>
<td>Small subpopulation affected</td>
</tr>
<tr>
<td>☐</td>
<td>Theoretical concern</td>
</tr>
<tr>
<td>☐</td>
<td>Other</td>
</tr>
</tbody>
</table>

N/A

2. Describe the particular review issue and the goal of the study/clinical trial. If the study/clinical trial is a FDAAA PMR, describe the risk. If the FDAAA PMR is created post-approval, describe the “new safety information.”
3. If the study/clinical trial is a **PMR**, check the applicable regulation.  
   **If not a PMR, skip to 4.**  
   - **Which regulation?**  
     - [ ] Accelerated Approval (subpart H/E)  
     - [ ] Animal Efficacy Rule  
     - [ ] Pediatric Research Equity Act  
     - [x] FDAAA required safety study/clinical trial  
   - **If the PMR is a FDAAA safety study/clinical trial, does it: (check all that apply)**  
     - [x] Assess a known serious risk related to the use of the drug?  
     - [ ] Assess signals of serious risk related to the use of the drug?  
     - [ ] Identify an unexpected serious risk when available data indicate the potential for a serious risk?  
   - **If the PMR is a FDAAA safety study/clinical trial, will it be conducted as:**  
     - [ ] Analysis of spontaneous postmarketing adverse events?  
       *Do not select the above study/clinical trial type if:* such an analysis will not be sufficient to assess or identify a serious risk  
     - [ ] Analysis using pharmacovigilance system?  
       *Do not select the above study/clinical trial type if:* the new pharmacovigilance system that the FDA is required to establish under section 505(k)(3) has not yet been established and is thus not sufficient to assess this known serious risk, or has been established but is nevertheless not sufficient to assess or identify a serious risk  
     - [x] Study: all other investigations, such as investigations in humans that are not clinical trials as defined below (e.g., observational epidemiologic studies), animal studies, and laboratory experiments?  
       *Do not select the above study type if:* a study will not be sufficient to identify or assess a serious risk  
   - [ ] Clinical trial: any prospective investigation in which the sponsor or investigator determines the method of assigning investigational product or other interventions to one or more human subjects?  

4. What type of study or clinical trial is required or agreed upon (describe and check type below)? If the study or trial will be performed in a subpopulation, list here.  

A prospective surveillance study over a five-year period on the in vitro susceptibility of target bacterial species to delafloxacin.
Required

☐ Observational pharmacoepidemiologic study
☐ Registry studies
☐ Primary safety study or clinical trial
☐ Pharmacogenetic or pharmacogenomic study or clinical trial if required to further assess safety
☐ Thorough Q-T clinical trial
☐ Nonclinical (animal) safety study (e.g., carcinogenicity, reproductive toxicology)
☒ Nonclinical study (laboratory resistance, receptor affinity, quality study related to safety)
☐ Pharmacokinetic studies or clinical trials
☐ Drug interaction or bioavailability studies or clinical trials
☐ Dosing trials

(Continuation of Question 4)

☐ Additional data or analysis required for a previously submitted or expected study/clinical trial
   (provide explanation)

☐ Meta-analysis or pooled analysis of previous studies/clinical trials
☐ Immunogenicity as a marker of safety
☐ Other (provide explanation)

Agreed upon:

☐ Quality study without a safety endpoint (e.g., manufacturing, stability)
☐ Pharmacoepidemiologic study not related to safe drug use (e.g., natural history of disease, background rates of adverse events)
☐ Clinical trials primarily designed to further define efficacy (e.g., in another condition, different disease severity, or subgroup) that are NOT required under Subpart H/E
☐ Dose-response study or clinical trial performed for effectiveness
☐ Nonclinical study, not safety-related (specify)

☐ Other

5. Is the PMR/PMC clear, feasible, and appropriate?

☒ Does the study/clinical trial meet criteria for PMRs or PMCs?
☒ Are the objectives clear from the description of the PMR/PMC?
☒ Has the applicant adequately justified the choice of schedule milestone dates?
☒ Has the applicant had sufficient time to review the PMRs/PMCs, ask questions, determine feasibility, and contribute to the development process?

☐ Check if this form describes a FDAAA PMR that is a randomized controlled clinical trial

*If so, does the clinical trial meet the following criteria?*

☐ There is a significant question about the public health risks of an approved drug
☐ There is not enough existing information to assess these risks
☐ Information cannot be gained through a different kind of investigation
☐ The trial will be appropriately designed to answer question about a drug’s efficacy and safety, and
☐ The trial will emphasize risk minimization for participants as the protocol is developed
This PMR/PMC has been reviewed for clarity and consistency, and is necessary to further refine the safety, efficacy, or optimal use of a drug, or to ensure consistency and reliability of drug quality.
This template should be completed by the PMR/PMC Development Coordinator and included for each PMR/PMC in the Action Package.

NDA Product Name: NDA 208610 & NDA 208611 Baxdela (delafloxacin) 450 mg Tablets (NDA 208610) and Baxdela (delafloxacin) 300 mg Injection (NDA 208611).

PMR/PMC Description: 3220-2: Conduct a tissue distribution study in pregnant rats treated during the period of organogenesis with the oral formulation and with the intravenous formulation of BAXDELA with the excipient sulfobutylether beta-cyclodextrin (SBEC) to assess the distribution of the drug substance to the reproductive tract and developing fetus.

PMR/PMC Schedule Milestones: Final Protocol Submission: 10/2017
Study/Trial Completion: 03/2018
Final Report Submission: 06/2018

6. During application review, explain why this issue is appropriate for a PMR/PMC instead of a pre-approval requirement. Check type below and describe.

☐ Unmet need
☐ Life-threatening condition
☐ Long-term data needed
☐ Only feasible to conduct post-approval
☐ Prior clinical experience indicates safety
☐ Small subpopulation affected
☒ Theoretical concern
☐ Other

An embryo-fetal developmental toxicology study has been performed using the oral delafloxacin formulation. It is unknown at this time whether or not tissue distribution and fetal exposure might be altered using the intravenous formulation containing sulfobutylether beta-cyclodextrin (SBEC), or if embryo-fetal development could be impacted by altered tissue distribution. If fetal exposure is increased, NOAEL doses may be lower, and the margin of safety for patients could be decreased.

7. Describe the particular review issue and the goal of the study/clinical trial. If the study/clinical trial is a FDAAA PMR, describe the risk. If the FDAAA PMR is created post-approval, describe the “new safety information.”
8. If the study/clinical trial is a PMR, check the applicable regulation. 
If not a PMR, skip to 4.

- Which regulation?
  - □ Accelerated Approval (subpart H/E)
  - □ Animal Efficacy Rule
  - □ Pediatric Research Equity Act
  - □ FDAAA required safety study/clinical trial

- If the PMR is a FDAAA safety study/clinical trial, does it: (check all that apply)
  - □ Assess a known serious risk related to the use of the drug?
  - □ Assess signals of serious risk related to the use of the drug?
  - □ Identify an unexpected serious risk when available data indicate the potential for a serious risk?

- If the PMR is a FDAAA safety study/clinical trial, will it be conducted as:
  - □ Analysis of spontaneous postmarketing adverse events?
    *Do not select the above study/clinical trial type if:* such an analysis will not be sufficient to assess or identify a serious risk
  - □ Analysis using pharmacovigilance system?
    *Do not select the above study/clinical trial type if:* the new pharmacovigilance system that the FDA is required to establish under section 505(k)(3) has not yet been established and is thus not sufficient to assess this known serious risk, or has been established but is nevertheless not sufficient to assess or identify a serious risk
  - □ Study: all other investigations, such as investigations in humans that are not clinical trials as defined below (e.g., observational epidemiologic studies), animal studies, and laboratory experiments?
    *Do not select the above study type if:* a study will not be sufficient to identify or assess a serious risk
  - □ Clinical trial: any prospective investigation in which the sponsor or investigator determines the method of assigning investigational product or other interventions to one or more human subjects?

9. What type of study or clinical trial is required or agreed upon (describe and check type below)? If the study or trial will be performed in a subpopulation, list here.

The study should determine if SBECID alters tissue distribution and potential fetal exposure to delafloxacin.
Required

- Observational pharmacoepidemiologic study
- Registry studies
- Primary safety study or clinical trial
- Pharmacogenetic or pharmacogenomic study or clinical trial if required to further assess safety
- Thorough Q-T clinical trial
- Nonclinical (animal) safety study (e.g., carcinogenicity, reproductive toxicology)
- Nonclinical study (laboratory resistance, receptor affinity, quality study related to safety)
- Pharmacokinetic studies or clinical trials
- Drug interaction or bioavailability studies or clinical trials
- Dosing trials

Continuation of Question 4

- Additional data or analysis required for a previously submitted or expected study/clinical trial (provide explanation)
- Meta-analysis or pooled analysis of previous studies/clinical trials
- Immunogenicity as a marker of safety
- Other (provide explanation)

Agreed upon:

- Quality study without a safety endpoint (e.g., manufacturing, stability)
- Pharmacoepidemiologic study not related to safe drug use (e.g., natural history of disease, background rates of adverse events)
- Clinical trials primarily designed to further define efficacy (e.g., in another condition, different disease severity, or subgroup) that are NOT required under Subpart H/E
- Dose-response study or clinical trial performed for effectiveness
- Nonclinical study, not safety-related (specify)

  Nonclinical tissue distribution study of the clinical intravenous formulation of delafloxacin in pregnant rats; if a difference is shown relative to the oral formulation, then an embryo-fetal developmental toxicology study will be performed.

- Other

10. Is the PMR/PMC clear, feasible, and appropriate?

  ☒ Does the study/clinical trial meet criteria for PMRs or PMCs?
  ☒ Are the objectives clear from the description of the PMR/PMC?
  ☒ Has the applicant adequately justified the choice of schedule milestone dates?
  ☒ Has the applicant had sufficient time to review the PMRs/PMCs, ask questions, determine feasibility, and contribute to the development process?

  ☐ Check if this form describes a FDAAA PMR that is a randomized controlled clinical trial

  If so, does the clinical trial meet the following criteria?

  ☐ There is a significant question about the public health risks of an approved drug
  ☐ There is not enough existing information to assess these risks
  ☐ Information cannot be gained through a different kind of investigation
The trial will be appropriately designed to answer questions about a drug’s efficacy and safety, and the trial will emphasize risk minimization for participants as the protocol is developed.

PMR/PMC Development Coordinator:

This PMR/PMC has been reviewed for clarity and consistency, and is necessary to further refine the safety, efficacy, or optimal use of a drug, or to ensure consistency and reliability of drug quality.
PMR/PMC Development Template

This template should be completed by the PMR/PMC Development Coordinator and included for each PMR/PMC in the Action Package.

PMR/PMC Schedule Milestones:

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final Protocol Submission</td>
<td>07/2018</td>
</tr>
<tr>
<td>Study/Trial Completion</td>
<td>01/2019</td>
</tr>
<tr>
<td>Final Report Submission</td>
<td>04/2019</td>
</tr>
</tbody>
</table>

11. During application review, explain why this issue is appropriate for a PMR/PMC instead of a pre-approval requirement. Check type below and describe.

- [ ] Unmet need
- [ ] Life-threatening condition
- [ ] Long-term data needed
- [x] Only feasible to conduct post-approval
- [ ] Prior clinical experience indicates safety
- [ ] Small subpopulation affected
- [ ] Theoretical concern
- [ ] Other

An embryo-fetal developmental toxicology study has been performed using the oral delafloxacin formulation. It is unknown at this time whether or not tissue distribution and fetal exposure might be altered using the intravenous formulation containing sulfobutylether beta-cyclodextrin (SBECD), or if embryo-fetal development could be impacted by altered tissue distribution. If fetal exposure is increased, NOAEL doses may be lower, and the margin of safety for patients could be decreased.

NDA/BLA #
Product Name: NDA 208610 & NDA 208611
Baxdela (delafloxacin) 450 mg Tablets (NDA 208610) and Baxdela (delafloxacin) 300 mg Injection (NDA 208611).

PMR/PMC Description: 3220-3: If the results of the tissue distribution studies from 3220-2 demonstrate greater exposure of the fetus / maternal reproductive tract to delafloxacin with the intravenous formulation, conduct an embryo-fetal developmental toxicology study in pregnant rats treated during the period of organogenesis with the intravenous formulation of BAXDELA to identify possible effects of delafloxacin with the excipient sulfobutylether beta-cyclodextrin (SBECD) on fetal development during the period of organogenesis.
12. Describe the particular review issue and the goal of the study/clinical trial. If the study/clinical trial is a FDAAA PMR, describe the risk. If the FDAAA PMR is created post-approval, describe the “new safety information.”

If there is increased exposure of the fetus and/or reproductive organs to delafloxacin, should determine if this altered exposure impacts embryo-fetal development and should determine the safety margin for intravenous delafloxacin for pregnant patients.

13. If the study/clinical trial is a PMR, check the applicable regulation. If not a PMR, skip to 4.

If not a PMR, skip to 4.

- Which regulation?
  - Accelerated Approval (subpart H/E)
  - Animal Efficacy Rule
  - Pediatric Research Equity Act
  - FDAAA required safety study/clinical trial

- If the PMR is a FDAAA safety study/clinical trial, does it: (check all that apply)
  - Assess a known serious risk related to the use of the drug?
  - Assess signals of serious risk related to the use of the drug?
  - Identify an unexpected serious risk when available data indicate the potential for a serious risk?

- If the PMR is a FDAAA safety study/clinical trial, will it be conducted as:
  - Analysis of spontaneous postmarketing adverse events?
    *Do not select the above study/clinical trial type if:* such an analysis will not be sufficient to assess or identify a serious risk
  - Analysis using pharmacovigilance system?
    *Do not select the above study/clinical trial type if:* the new pharmacovigilance system that the FDA is required to establish under section 505(k)(3) has not yet been established and is thus not sufficient to assess this known serious risk, or has been established but is nevertheless not sufficient to assess or identify a serious risk

- Study: all other investigations, such as investigations in humans that are not clinical trials as defined below (e.g., observational epidemiologic studies), animal studies, and laboratory experiments?
  *Do not select the above study type if:* a study will not be sufficient to identify or assess a serious risk

- Clinical trial: any prospective investigation in which the sponsor or investigator determines the method of assigning investigational product or other interventions to one or more human subjects?

14. What type of study or clinical trial is required or agreed upon (describe and check type below)? If the study or trial will be performed in a subpopulation, list here.

The study will be a nonclinical study in pregnant animals to determine the effect of delafloxacin in the intravenous formulation containing SBECOD on embryo-fetal development.
Required

- Observational pharmacoepidemiologic study
- Registry studies
- Primary safety study or clinical trial
- Pharmacogenetic or pharmacogenomic study or clinical trial if required to further assess safety
- Thorough Q-T clinical trial
- Nonclinical (animal) safety study (e.g., carcinogenicity, reproductive toxicology)
- Nonclinical study (laboratory resistance, receptor affinity, quality study related to safety)
- Pharmacokinetic studies or clinical trials
- Drug interaction or bioavailability studies or clinical trials
- Dosing trials

Continuation of Question 4

- Additional data or analysis required for a previously submitted or expected study/clinical trial (provide explanation)
- Meta-analysis or pooled analysis of previous studies/clinical trials
- Immunogenicity as a marker of safety
- Other (provide explanation)

Agreed upon:

- Quality study without a safety endpoint (e.g., manufacturing, stability)
- Pharmacoepidemiologic study not related to safe drug use (e.g., natural history of disease, background rates of adverse events)
- Clinical trials primarily designed to further define efficacy (e.g., in another condition, different disease severity, or subgroup) that are NOT required under Subpart H/E
- Dose-response study or clinical trial performed for effectiveness
- Nonclinical study, not safety-related (specify)

Nonclinical tissue distribution study of the clinical intravenous formulation of delafloxacin in pregnant rats; if a difference is shown relative to the oral formulation, then an embryo-fetal developmental toxicology study will be performed.

- Other
  Nonclinical tissue distribution study of the clinical intravenous formulation of delafloxacin in pregnant rats; if a difference is shown relative to the oral formulation, then an embryo-fetal developmental toxicology study will be performed.

15. Is the PMR/PMC clear, feasible, and appropriate?

- Does the study/clinical trial meet criteria for PMRs or PMCs?
- Are the objectives clear from the description of the PMR/PMC?
- Has the applicant adequately justified the choice of schedule milestone dates?
- Has the applicant had sufficient time to review the PMRs/PMCs, ask questions, determine feasibility, and contribute to the development process?

- Check if this form describes a FDAAA PMR that is a randomized controlled clinical trial

*If so, does the clinical trial meet the following criteria?*
☐ There is a significant question about the public health risks of an approved drug
☐ There is not enough existing information to assess these risks
☐ Information cannot be gained through a different kind of investigation
☐ The trial will be appropriately designed to answer question about a drug’s efficacy and safety, and
☐ The trial will emphasize risk minimization for participants as the protocol is developed

PMR/PMC Development Coordinator:
☒ This PMR/PMC has been reviewed for clarity and consistency, and is necessary to further refine the safety, efficacy, or optimal use of a drug, or to ensure consistency and reliability of drug quality.
PMR/PMC Development Template: Product Quality (CMC)

This template should be completed by the review chemist (OPQ) or biologist (OBP) and included for each type of CMC PMR/PMC in the Action Package. See #4 for a list of CMC PMR/PMC types.

NDA/BLA #   208610
Product Name: Baxdela (delafloxacin) 450 mg Tablets (NDA 208610) and Baxdela (delafloxacin) 300 mg Injection (NDA 208611).

PMC Description: 3220-4: Add the facility responsible for XRPD testing. The filing category should be selected based on FDA Guidance (See: Guidance for Industry Changes to an Approved NDA or ANDA).

PMC Schedule Milestones:

Final Protocol Submission: Submitted
Study/Trial Completion: 08/01/2017
Final Report Submission: 09/01/2017

PMC Description: 3220-5: Establish a validated XRPD limit test as part of product release. This information should be submitted as Changes Being Effected-30 Supplement.

PMC Schedule Milestones:

Final Protocol Submission: Submitted
Study/Trial Completion: 08/01/2017
Final Report Submission: 09/01/2017

PMC Description: 3220-6: Update drug product release specifications so commercial batches will have XRPD testing to confirm polymorphic form as a part of drug product final release testing. This information should be submitted as Changes Being Effected-30 Supplement.

PMC Schedule Milestones:

Final Protocol Submission: Submitted
Study/Trial Completion: 08/01/2017
Final Report Submission: 09/01/2017

ADD MORE AS NEEDED USING THE SAME TABULAR FORMAT FOR EACH PMC.

INCLUDE DESCRIPTIONS AND MILESTONES IN THE TABLE ABOVE FOR ALL CMC/OBP NON-REPORTABLE PMCS FOR WHICH THE FOLLOWING ANSWERS WILL BE IDENTICAL. USE A SEPARATE TEMPLATE FOR EACH PMR/PMC FOR WHICH THE ANSWERS TO THE FOLLOWING QUESTIONS DIFFER.

DO NOT USE THIS FORM IF ANY STUDIES WILL BE REQUIRED UNDER FDAAA OR WILL BE PUBLICLY REPORTABLE.

1. During application review, explain why this issue is appropriate for a PMC instead of a pre-approval requirement. Check reason below and describe.
2. Describe the particular review issue and the goal of the study.

Based on the information presented in the NDA, the polymorphic form of the drug substance in the drug product is expected to have a low probability to negatively impact the drug product quality. However, a drug substance polymorphic form control as part of the drug product specifications will provide additional assurance of quality for the drug product.

The goal of the proposed PMC study is to establish as part of the drug product specifications a validated analytical method (XRD) with well-justified acceptance limits on the polymorphic form of the drug substance in the drug product. Additionally, the applicant will also identify a GMP facility which will be responsible for polymorph testing.

3. [OMIT – for PMRs only]

4. What type of study is agreed upon (describe and check type below)?

   Select only one. Fill out a new sheet for each type of PMR/PMC study.

   □ Dissolution testing
   □ Assay
Sterility
Potency
Product delivery
Drug substance characterization
Intermediates characterization
Impurity characterization
Reformulation
Manufacturing process issues
Other

Describe the agreed-upon study:

The company has agreed to:
   a) Monitor polymorphic forms via XRD
   b) Establish a validated XRD limit test
   c) Include a test for polymorph control in the drug product specification
   d) Identify a GMP testing facility to perform this test

5. To be completed by OPQ/OBP Manager:
   - Does the study meet criteria for PMCs?
   - Are the objectives clear from the description of the PMC?
   - Has the applicant adequately justified the choice of schedule milestone dates?
   - Has the applicant had sufficient time to review the PMCs, ask questions, determine feasibility, and contribute to the development process?

PMR/PMC Development Coordinator:
   - This PMR/PMC has been reviewed for clarity and consistency, and is necessary to further refine the safety, efficacy, or optimal use of a drug, or to ensure consistency and reliability of drug quality.
PMR/PMC Development Template: Product Quality (CMC)

This template should be completed by the review chemist (OPQ) or biologist (OBP) and included for each type of CMC PMR/PMC in the Action Package. See #4 for a list of CMC PMR/PMC types.

NDA/BLA #: 208611
Product Name: Baxdela (delafoxacin) 300 mg Injection (NDA 208611)

PMC Description: 3320-7: Provide results from the on-going requalification of the sterility test method per USP <71>. Sponsor to provide data collected from on-going PV (process validation) runs.

PMC Schedule Milestones: Final Protocol Submission: Submitted
Study/Trial Completion: 08/01/2017
Final Report Submission: 09/01/2017

PMC Description: 3220-8: Provide PV data to support a more suitable In-Process Control (IPC) limit at \( \frac{\text{[]}%}{\text{[]}%} \) as a CBE-30 in lieu of the proposed specification (\( \frac{\text{[]}%}{\text{[]}\text{mg/mL}} \) ) of target, in NDA 208611.

PMC Schedule Milestones: Final Protocol Submission: Submitted
Study/Trial Completion: 08/01/2017
Final Report Submission: 09/01/2017

- ADD MORE AS NEEDED USING THE SAME TABULAR FORMAT FOR EACH PMC.
- INCLUDE DESCRIPTIONS AND MILESTONES IN THE TABLE ABOVE FOR ALL CMC/OBP NON-REPORTABLE PMCS FOR WHICH THE FOLLOWING ANSWERS WILL BE IDENTICAL. USE A SEPARATE TEMPLATE FOR EACH PMR/PMC FOR WHICH THE ANSWERS TO THE FOLLOWING QUESTIONS DIFFER.
- DO NOT USE THIS FORM IF ANY STUDIES WILL BE REQUIRED UNDER FFADA OR WILL BE PUBLICLY REPORTABLE

1. During application review, explain why this issue is appropriate for a PMC instead of a pre-approval requirement. Check reason below and describe.

- [ ] Need for drug (unmet need/life-threatening condition)
- [ ] Long-term data needed (e.g., stability data)
- [ ] Only feasible to conduct post-approval
- [X] Improvements to methods
- [ ] Theoretical concern
- [X] Manufacturing process analysis
- [ ] Other

The NDA provides for delafloxacin lyophilized powder for injection for the treatment of Acute Bacterial Skin and Skin Structure Infection in adults. The recommended studies, as discussed below, will provide further assurance on the quality of the product.
2. Describe the particular review issue and the goal of the study.

In the original submission, the applicant included in-process specification for % assay at \( \text{[(b) (4)]} \% \) of the \( \text{[(b) (4)]} \) volume with limits between \( \text{[(b) (4)]} \% \) of \( \text{[(b) (4)]} \) mg/mL. The in-process assay test is conducted \( \text{[(b) (4)]} \) to ensure that the drug concentration \( \text{[(b) (4)]} \) is within acceptable limits. However, in an email communication to RBPM dated 03/27/2017, the applicant asked if provisional acceptance criteria for in-process assay limits can be set at \( \text{[(b) (4)]} \% \) until completion of the process validation batches. If the process validation data supports the tighter limits, then the limits will be revised and submitted as CBE-30. In the meantime, the final release specifications for the product will remain unchanged.

Initial method suitability for sterility testing was performed by the applicant using only 2 vials of drug product, which did not comply with the USP <71> requirement for the number of vials to be tested based on the production batch size. An information request was issued advising the applicant that sterility testing method suitability should be repeated to conform with USP <71> requirements. The applicant’s response to the IR was unclear, so a 15 February 2017 teleconference was scheduled to clarify how they intended to perform method suitability. At the conclusion of the teleconference, the applicant agreed to submit a revised sterility testing protocol to satisfy USP <71> (submitted 24 February 2017). However, method suitability could not be performed until new batches of drug product were produced; the applicant has committed to performing sterility testing method suitability per the submitted protocol once drug product is produced \( \text{[(b) (4)]} \). The goal of the PMC study is to establish the suitability of the proposed sterility testing method for sterility testing of the drug product in compliance with USP <71>.

3. [OMIT – for PMRs only]

4. What type of study is agreed upon (describe and check type below)?

Select only one. Fill out a new sheet for each type of PMR/PMC study.

- Dissolution testing
- Assay
- Sterility
- Potency
- Product delivery
- Drug substance characterization
- Intermediates characterization
- Impurity characterization
- Reformulation
- Manufacturing process issues
- Other

Describe the agreed-upon study:

The company has agreed to:

a) Requalify the sterility test
b) Revise the IPC limit for assay
5. To be completed by OPQ/OBP Manager:

☑ Does the study meet criteria for PMCs?
☑ Are the objectives clear from the description of the PMC?
☑ Has the applicant adequately justified the choice of schedule milestone dates?
☑ Has the applicant had sufficient time to review the PMCs, ask questions, determine feasibility, and contribute to the development process?

PMR/PMC Development Coordinator:

☑ This PMR/PMC has been reviewed for clarity and consistency, and is necessary to further refine the safety, efficacy, or optimal use of a drug, or to ensure consistency and reliability of drug quality.
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
06/14/2017

JOSEPH G TOERNER
06/14/2017
Division of Anti-infective Products

REGULATORY PROJECT MANAGER LABELING REVIEW

Application: NDA 208610 & 208611
Name of Drug: Baxdela (delafloxacin) 450 mg Tablets & Baxdela (delafloxacin) Injection
Applicant: Melinta Pharmaceuticals

Labeling Reviewed

Submission Date: 10-19-17
Receipt Date: 10-19-17

Background and Summary Description: Melinta submitted NDA 208610, BAXDELA™ (delafloxacin) 450 mg Tablets and delafloxacin IV injections as original 505(b)(1) applications, in support of the indication for Acute Bacterial Skin and Skin Structure Infection (ABSSSI). The labeling section of these applications includes the Prescribing Information, MedGuide, Carton & Container, and the blister cards.

Review
This review is based on the applicant’s submitted Word format of the prescribing information (PI) and MedGuide. The applicant’s proposed PI was reviewed in accordance with the labeling format requirements listed in the “Selected Requirements of Prescribing Information (SRPI)” checklist. DMEPA, OPDP & PLT were consulted to review the PI, MED Guide and Carton & Container.

Recommendations
No SRPI format deficiencies were identified in the review of this PI

<table>
<thead>
<tr>
<th>Fariba Izadi</th>
<th>05-31-17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory Project Manager</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Carmen DeBellas</th>
<th>06-01-17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chief, Project Management Staff</td>
<td></td>
</tr>
</tbody>
</table>
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/s/

FARIBA IZADI
06/06/2017

CARMEN L DEBELLAS
06/06/2017
REGULATORY PROJECT MANAGER
PHYSICIAN LABELING RULE (PLR) FORMAT REVIEW
OF THE PRESCRIBING INFORMATION

Complete for all new NDAs, BLAs, Efficacy Supplements, and PLR Conversion Labeling Supplements

Application: NDA # 208610 & 208611

Application Type: New NDAs- NME 1

Drug Name(s)/Dosage Form(s): Delafloxacin

Applicant: Melinta Therapeutics

Receipt Date: 11-19-16

Goal Date: 06-19-17

1. Regulatory History and Applicant’s Main Proposals
Melinta is submitting NDA 208610, BAXDELA™ (delafloxacin) 450 mg Tablets and delafloxacin IV injections as original 505(b)(1) applications, to support the indication for Acute Bacterial Skin and Skin Structure Infection (ABSSSI).

2. Review of the Prescribing Information
This review is based on the applicant’s submitted Word format of the prescribing information (PI). The applicant’s proposed PI was reviewed in accordance with the labeling format requirements listed in the “Selected Requirements of Prescribing Information (SRPI)” checklist (see Section 4 of this review).

3. Conclusions/Recommendations
No SRPI format deficiencies were identified in the review of this PI.
Highlights

See Appendix for a sample tool illustrating Highlights format.

HIGHLIGHTS GENERAL FORMAT

| YES | 1. Highlights (HL) must be in a minimum of 8-point font and should be in two-column format, with ½ inch margins on all sides and between columns. |
| Comment: |
| YES | 2. The length of HL must be one-half page or less unless a waiver has been granted in a previous submission. The HL Boxed Warning does not count against the one-half page requirement. Instructions to complete this item: If the length of the HL is one-half page or less, select “YES” in the drop-down menu because this item meets the requirement. However, if HL is longer than one-half page, select “NO” unless a waiver has been granted. |
| Comment: |
| YES | 3. A horizontal line must separate: |
| • HL from the Table of Contents (TOC), and |
| • TOC from the Full Prescribing Information (FPI). |
| Comment: |
| YES | 4. All headings in HL (from Recent Major Changes to Use in Specific Populations) must be bolded and presented in the center of a horizontal line. (Each horizontal line should extend over the entire width of the column.) The HL headings (from Recent Major Changes to Use in Specific Populations) should be in UPPER CASE letters. See Appendix for HL format. |
| Comment: |
| YES | 5. White space should be present before each major heading in HL. There must be no white space between the HL Heading and HL Limitation Statement. There must be no white space between the product title and Initial U.S. Approval. See Appendix for HL format. |
| Comment: |
| YES | 6. Each summarized statement or topic in HL must reference the section(s) or subsection(s) of the Full Prescribing Information (FPI) that contain more detailed information. The preferred format is the numerical identifier in parenthesis [e.g., (1.1)] at the end of each summarized statement or topic. |
| Comment: |
| YES | 7. Headings in HL must be presented in the following order: |

<table>
<thead>
<tr>
<th>Heading</th>
<th>Required/Optional</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Highlights Heading</td>
<td>Required</td>
</tr>
<tr>
<td>• Highlights Limitation Statement</td>
<td>Required</td>
</tr>
<tr>
<td>• Product Title</td>
<td>Required</td>
</tr>
<tr>
<td>• Initial U.S. Approval</td>
<td>Required</td>
</tr>
<tr>
<td>• Boxed Warning</td>
<td>Required if a BOXED WARNING is in the FPI</td>
</tr>
<tr>
<td>• Recent Major Changes</td>
<td>Required for only certain changes to PI*</td>
</tr>
<tr>
<td>• Indications and Usage</td>
<td>Required</td>
</tr>
<tr>
<td>• Dosage and Administration</td>
<td>Required</td>
</tr>
</tbody>
</table>
Selected Requirements of Prescribing Information

<table>
<thead>
<tr>
<th>Requirements</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>• DOSAGE FORMS AND STRENGTHS</td>
<td>Required</td>
</tr>
<tr>
<td>• CONTRAINDICATIONS</td>
<td>Required</td>
</tr>
<tr>
<td>• WARNINGS AND PRECAUTIONS</td>
<td>Required</td>
</tr>
<tr>
<td>• ADVERSE REACTIONS</td>
<td>Required</td>
</tr>
<tr>
<td>• DRUG INTERACTIONS</td>
<td>Optional</td>
</tr>
<tr>
<td>• USE IN SPECIFIC POPULATIONS</td>
<td>Optional</td>
</tr>
<tr>
<td>• PATIENT COUNSELING INFORMATION STATEMENT</td>
<td>Required</td>
</tr>
<tr>
<td>• REVISION DATE</td>
<td>Required</td>
</tr>
</tbody>
</table>

* RMC only applies to five labeling sections in the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS.

Comment:

HIGHLIGHTS DETAILS

Highlights Heading

YES 8. At the beginning of HL, the following heading, “HIGHLIGHTS OF PRESCRIBING INFORMATION” must be bolded and should appear in all UPPER CASE letters.

Comment:

Highlights Limitation Statement

YES 9. The bolded HL Limitation Statement must include the following verbatim statement: “These highlights do not include all the information needed to use (insert NAME OF DRUG PRODUCT) safely and effectively. See full prescribing information for (insert NAME OF DRUG PRODUCT).” The name of drug product should appear in UPPER CASE letters.

Comment:

Product Title in Highlights

YES 10. Product title must be bolded.

Comment:

Initial U.S. Approval in Highlights

YES 11. Initial U.S. Approval must be bolded, and include the verbatim statement “Initial U.S. Approval:” followed by the 4-digit year.

Comment:

Boxed Warning (BW) in Highlights

YES 12. All text in the BW must be bolded.

Comment:

YES 13. The BW must have a title in UPPER CASE, following the word “WARNING” and other words to identify the subject of the warning. Even if there is more than one warning, the term “WARNING” and not “WARNINGS” should be used. For example: “WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE”. If there is more than one warning in the BW title, the word “and” in lower case can separate the warnings. The BW title should be centered.

Comment: And should be in lower case
Selected Requirements of Prescribing Information

**YES** 14. The BW must always have the verbatim statement “*See full prescribing information for complete boxed warning.*” This statement must be placed immediately beneath the BW title, and should be centered and appear in *italics*.

**Comment:**

**YES** 15. The BW must be limited in length to 20 lines. (This includes white space but does not include the BW title and the statement “*See full prescribing information for complete boxed warning.*”)

**Comment:**

Recent Major Changes (RMC) in Highlights

**N/A** 16. RMC pertains to only five sections of the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS. Labeling sections for RMC must be listed in the same order in HL as they appear in the FPI.

**Comment:**

**N/A** 17. The RMC must include the section heading(s) and, if appropriate, subsection heading(s) affected by the recent major change, together with each section’s identifying number and date (month/year format) on which the change was incorporated in the PI (supplement approval date). For example, “Warnings and Precautions, Acute Liver Failure (5.1) --- 8/2015.”

**Comment:**

**N/A** 18. A changed section must be listed under the RMC heading for at least one year after the date of the labeling change and must be removed at the first printing subsequent to the one year period. (No listing should be one year older than the revision date.)

**Comment:**

Dosage Forms and Strengths in Highlights

**YES** 19. For a product that has more than one dosage form (e.g., capsules, tablets, injection), bulleted headings should be used.

**Comment:**

Contraindications in Highlights

**YES** 20. All contraindications listed in the FPI must also be listed in HL. If there is more than one contraindication, each contraindication should be bulleted. If no contraindications are known, must include the word “None.”

**Comment:**

Adverse Reactions in Highlights

**YES** 21. For drug products other than vaccines, the verbatim **bolded** statement must be present: “To report SUSPECTED ADVERSE REACTIONS, contact (insert name of manufacturer) at
Selected Requirements of Prescribing Information

(insert manufacturer’s U.S. phone number which should be a toll-free number) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.”

Comment:

Patient Counseling Information Statement in Highlights

YES 22. The Patient Counseling Information statement must include one of the following three bolded verbatim statements that is most applicable:

If a product does not have FDA-approved patient labeling:

- See 17 for PATIENT COUNSELING INFORMATION

If a product has (or will have) FDA-approved patient labeling:

- See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling
- See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Comment:

Revision Date in Highlights

YES 23. The revision date must be at the end of HL, and should be bolded and right justified (e.g., “Revised: 8/2015”).

Comment:
Selected Requirements of Prescribing Information

Contents: Table of Contents (TOC)

See Appendix for a sample tool illustrating Table of Contents format.

YES 24. The TOC should be in a two-column format.

Comment:

YES 25. The following heading must appear at the beginning of the TOC: “FULL PRESCRIBING INFORMATION: CONTENTS.” This heading should be in all UPPER CASE letters and bolded.

Comment:

YES 26. The same title for the BW that appears in HL and the FPI must also appear at the beginning of the TOC in UPPER CASE letters and bolded.

Comment:

YES 27. In the TOC, all section headings must be bolded and should be in UPPER CASE.

Comment:

YES 28. In the TOC, all subsection headings must be indented and not bolded. The headings should be in title case [first letter of all words are capitalized except first letter of prepositions (for, of, to) and articles (a, an, the), or conjunctions (or, and)].

Comment:

YES 29. The section and subsection headings in the TOC must match the section and subsection headings in the FPI.

Comment:

YES 30. If a section or subsection required by regulation [21 CFR 201.56(d)(1)] is omitted from the FPI, the numbering in the TOC must not change. The heading “FULL PRESCRIBING INFORMATION: CONTENTS**” must be followed by an asterisk and the following statement must appear at the end of the TOC: “*Sections or subsections omitted from the full prescribing information are not listed.”

Comment:
Selected Requirements of Prescribing Information

Full Prescribing Information (FPI)

FULL PRESCRIBING INFORMATION: GENERAL FORMAT

**YES** 31. The **bolded** section and subsection headings in the FPI must be named and numbered in accordance with 21 CFR 201.56(d)(1) as noted below. (Section and subsection headings should be in UPPER CASE and title case, respectively.) If a section/subsection required by regulation is omitted, the numbering must not change. Additional subsection headings (i.e., those not named by regulation) must also be **bolded** and numbered.

<table>
<thead>
<tr>
<th>BOXED WARNING</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 INDICATIONS AND USAGE</td>
</tr>
<tr>
<td>2 DOSAGE AND ADMINISTRATION</td>
</tr>
<tr>
<td>3 DOSAGE FORMS AND STRENGTHS</td>
</tr>
<tr>
<td>4 CONTRAINDICATIONS</td>
</tr>
<tr>
<td>5 WARNINGS AND PRECAUTIONS</td>
</tr>
<tr>
<td>6 ADVERSE REACTIONS</td>
</tr>
<tr>
<td>7 DRUG INTERACTIONS</td>
</tr>
<tr>
<td>8 USE IN SPECIFIC POPULATIONS</td>
</tr>
<tr>
<td>8.1 Pregnancy</td>
</tr>
<tr>
<td>8.2 Lactation (if not required to be in Pregnancy and Lactation Labeling Rule (PLLR) format, use “Labor and Delivery”)</td>
</tr>
<tr>
<td>8.3 Females and Males of Reproductive Potential (if not required to be in PLLR format, use “Nursing Mothers”)</td>
</tr>
<tr>
<td>8.4 Pediatric Use</td>
</tr>
<tr>
<td>8.5 Geriatric Use</td>
</tr>
<tr>
<td>9 DRUG ABUSE AND DEPENDENCE</td>
</tr>
<tr>
<td>9.1 Controlled Substance</td>
</tr>
<tr>
<td>9.2 Abuse</td>
</tr>
<tr>
<td>9.3 Dependence</td>
</tr>
<tr>
<td>10 OVERDOSAGE</td>
</tr>
<tr>
<td>11 DESCRIPTION</td>
</tr>
<tr>
<td>12 CLINICAL PHARMACOLOGY</td>
</tr>
<tr>
<td>12.1 Mechanism of Action</td>
</tr>
<tr>
<td>12.2 Pharmacodynamics</td>
</tr>
<tr>
<td>12.3 Pharmacokinetics</td>
</tr>
<tr>
<td>12.4 Microbiology (by guidance)</td>
</tr>
<tr>
<td>12.5 Pharmacogenomics (by guidance)</td>
</tr>
<tr>
<td>13 NONCLINICAL TOXICOLOGY</td>
</tr>
<tr>
<td>13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility</td>
</tr>
<tr>
<td>13.2 Animal Toxicology and/or Pharmacology</td>
</tr>
<tr>
<td>14 CLINICAL STUDIES</td>
</tr>
<tr>
<td>15 REFERENCES</td>
</tr>
<tr>
<td>16 HOW SUPPLIED/STORAGE AND HANDLING</td>
</tr>
<tr>
<td>17 PATIENT COUNSELING INFORMATION</td>
</tr>
</tbody>
</table>

**Comment:**

**YES** 32. The preferred presentation for cross-references in the FPI is the section (not subsection) heading followed by the numerical identifier. The entire cross-reference should be in *italics* and enclosed within brackets. For example, “[see Warnings and Precautions (5.2)].”

**Comment:**
33. For each RMC listed in HL, the corresponding new or modified text in the FPI must be marked with a vertical line on the left edge.

Comment:

FULL PRESCRIBING INFORMATION DETAILS

FPI Heading

YES 34. The following heading “FULL PRESCRIBING INFORMATION” must be bolded, must appear at the beginning of the FPI, and should be in UPPER CASE.

Comment:

BOXED WARNING Section in the FPI

YES 35. All text in the BW should be bolded.

Comment:

YES 36. The BW must have a title in UPPER CASE, following the word “WARNING” and other words to identify the subject of the warning. (Even if there is more than one warning, the term, “WARNING” and not “WARNINGS” should be used.) For example: “WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE”. If there is more than one warning in the BW title, the word “and” in lower case can separate the warnings.

Comment: And should be in lower case

CONTRAINDICATIONS Section in the FPI

YES 37. If no Contraindications are known, this section must state “None.”

Comment:

ADVERSE REACTIONS Section in the FPI

YES 38. When clinical trials adverse reactions data are included (typically in the “Clinical Trials Experience” subsection), the following verbatim statement (or appropriate modification) should precede the presentation of adverse reactions from clinical trials:

“Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.”

Comment:

YES 39. When postmarketing adverse reaction data are included (typically in the “Postmarketing Experience” subsection), the following verbatim statement (or appropriate modification) should precede the presentation of adverse reactions:

“The following adverse reactions have been identified during post-approval use of (insert drug name). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.”

Comment:
PATIENT COUNSELING INFORMATION Section in the FPI

40. Must reference any FDA-approved patient labeling in Section 17 (PATIENT COUNSELING INFORMATION). The reference statement should appear at the beginning of Section 17 and include the type(s) of FDA-approved patient labeling (e.g., Patient Information, Instructions for Use, or Medication Guide). Recommended language for the reference statement should include one of the following five verbatim statements that is most applicable:

- Advise the patient to read the FDA-approved patient labeling (Patient Information).
- Advise the patient to read the FDA-approved patient labeling (Instructions for Use).
- Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).
- Advise the patient to read the FDA-approved patient labeling (Medication Guide).
- Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Comment: The word medication Guide is missing.

41. FDA-approved patient labeling (e.g., Patient Information, Instructions for Use, or Medication Guide) must not be included as a subsection under Section 17 (PATIENT COUNSELING INFORMATION). All FDA-approved patient labeling must appear at the end of the PI upon approval.

Comment:
Selected Requirements of Prescribing Information

Appendix: Highlights and Table of Contents Format

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PROPRIETARY NAME safely and effectively. See full prescribing information for PROPRIETARY NAME.

PROPRIETARY NAME (non-proprietary name) dosage form, route of administration, controlled substance symbol Initial U.S. Approval: YYYY

WARNING: TITLE OF WARNING
See full prescribing information for complete boxed warning.
- Text (4)
- Text (5.x)

RECENT MAJOR CHANGES
Section Title, Subsection Title (x.x) M/201Y
Section Title, Subsection Title (x.x) M/201Y

INDICATIONS AND USAGE
PROPRIETARY NAME is a (insert FDA established pharmacologic class text phrase) indicated for ... (1)
Limitations of Use: Text (1)

DOSEAGE AND ADMINISTRATION
- Text (2.x)
- Text (2.x)

DOSEAGE FORMS AND STRENGTHS
Dosage form(s); strength(s) (3)

CONTRAINDICATIONS
- Text (4)
- Text (4)

WARNINGS AND PRECAUTIONS
- Text (5.x)
- Text (5.x)

ADVERSE REACTIONS
Most common adverse reactions (incidence > x%) are text (5.x)
To report SUSPECTED ADVERSE REACTIONS, contact name of manufacturer at toll-free phone # or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS
- Text (7.x)
- Text (7.x)

USE IN SPECIFIC POPULATIONS
- Text (8.x)
- Text (6.x)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling OR and Medication Guide.

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: TITLE OF WARNING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
  2.1 Subsection Title
  2.2 Subsection Title
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
  5.1 Subsection Title
  5.2 Subsection Title
6 ADVERSE REACTIONS
  6.1 Clinical Trials Experience
  6.2 Immunogenicity
  6.2 or 6.3 Postmarketing Experience
7 DRUG INTERACTIONS
  7.1 Subsection Title
  7.2 Subsection Title
8 USE IN SPECIFIC POPULATIONS
  8.1 Pregnancy
  8.2 Lactation (if not required to be in PLLR format use Labor and Delivery)
  8.3 Females and Males of Reproductive Potential (if not required to be in PLLR format use Nursing Mothers)
  8.4 Pediatric Use
  8.5 Geriatric Use
  8.6 Subpopulation X

9 DRUG ABUSE AND DEPENDENCE
  9.1 Controlled Substance
  9.2 Abuse
  9.3 Dependence
10 OVERDOSE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
  12.1 Mechanism of Action
  12.2 Pharmacodynamics
  12.3 Pharmacokinetics
  12.4 Microbiology
  12.5 Pharmacogenomics
13 NONCLINICAL TOXICOLOGY
  13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
  13.2 Animal Toxicology and/or Pharmacology
14 CLINICAL STUDIES
  14.1 Subsection Title
  14.2 Subsection Title
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION
* Sections or subsections omitted from the full prescribing information are not listed.
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
05/15/2017
Clinical Inspection Summary
NDAs 208610 & 208611, [Delafloxacin]

Clinical Inspection Summary

<table>
<thead>
<tr>
<th>Date</th>
<th>April 26, 2017</th>
</tr>
</thead>
</table>
| From         | Bei Yu, Ph.D., Reviewer  
Janice K. Pohlman, M.D., M.P.H., Team Leader  
Kassa Ayalew, M.D., M.P.H., Branch Chief  
Good Clinical Practice Assessment Branch  
Division of Clinical Compliance Evaluation  
Office of Scientific Investigations |
| To           | Fariba Izadi, Project Manager  
Caroline Jjingo, Medical Officer  
Thomas Smith, Team Leader  
Division of Anti- Infective Products |
| NDA/BLA #    | NDAs 208610 & 208611 |
| Applicant    | Melinta Therapeutics, Inc. |
| Drug         | Delafloxacin |
| NME (Yes/No) | Yes |
| Therapeutic Classification | Priority Review |
| Proposed Indication(s) | Treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria |
| Consultation Request Date | 5/8/2017 |
| Summary Goal Date | 5/8/2017 |
| Action Goal Date | 6/19/2017 |
| PDUFA Date    | 6/19/2017 |

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

The clinical sites of Drs. Hansen, Overcash, Green, and Farley were inspected in support of these NDAs. In addition, the sponsor, Melinta Therapeutics, Inc., was also inspected.

The studies appear to have been conducted adequately, and the data generated by these sites and as submitted by the sponsor appear acceptable in support of the respective indication. Although there were regulatory violations observed at the Drs. Hansen and Overcash sites, the observations do not appear to have significant impact on subject safety or efficacy assessment.

The final classification of the inspections of Drs. Farley and Green is No Action Indicated (NAI), and Dr. Hansen is Voluntary Action Indicated (VAI). The preliminary classification of the inspection of Dr. Overcash is VAI. The preliminary classification of the inspection of the sponsor, Melinta, is NAI. The inspection observations for Dr. Overcash’s clinical investigator site are based upon preliminary communications with the ORA investigator and the Form FDA 483. The inspection observations for the sponsor are based upon preliminary communications.

Reference ID: 4094909
with the ORA investigator. If a significant change in regulatory classification is determined after submission and review of the Establishment Inspection Report (EIR), an addendum to this clinical inspection summary will be provided.

II. BACKGROUND

The Applicant submitted the NDAs to support the use of delafloxacin intravenous (IV) infusion or oral tablet in the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria in adults.

The following two pivotal study protocols were inspected in support of this application:

**Study RX-3341-302:** A Phase 3, Multicenter, Randomized, Double-Blind, Active-Controlled Study to Evaluate the Efficacy and Safety of Delafloxacin Compared with Vancomycin + Aztreonam in Patients with Acute Bacterial Skin and Skin Structure Infections

This was a randomized, double-blind, multicenter study, to assess the clinical efficacy of delafloxacin compared with vancomycin + aztreonam in patients with ABSSSIs at 48 to 72 hours after initiation of treatment. Patients who met the criteria were randomly assigned to 1 of 2 treatment arms in a 1:1 ratio to receive either delafloxacin 300 mg IV every 12 hours or vancomycin 15 mg/kg IV every 12 hours based on actual body weight for a total of 10-28 doses based on the investigator’s judgment. The primary efficacy endpoint was a ≥ 20% reduction in lesion erythema area at 48 to 72 hours after initiation of treatment compared to baseline as determined by digital measurements of the leading edge of the affected site.

The study was conducted at 34 clinical sites in 7 countries including the US between 4/25/2013 and 6/6/2014. A total of 660 patients were enrolled and 547 patients completed the study.

Two clinical sites were selected for inspection:
Dr. Overcash’s site was selected for inspection mainly because of high enrollment, and high site efficacy effect; in addition, the site shared the same address with Dr. Green’s site for Study 303.

Dr. Farley’s site was selected for inspection mainly because of high site efficacy effect, and high events of serious adverse events (SAE), with four SAEs in the study drug arm.

**Study RX-3341-303:** A Phase 3, Multicenter, Randomized, Double-Blind, Active-Controlled Study to Evaluate the Efficacy and Safety of IV Oral Delafloxacin Compared with Vancomycin + Aztreonam in Patients with Acute Bacterial Skin and Skin Structure Infections

The study was identical to Study 302 in study design and methodologies. However, Study 303 used the IV formulation for 6 doses, then all patients in the delafloxacin group had a mandatory switch to delafloxacin 450 mg orally Q12h. Study 303 also included patients with severe renal impairment (CrCl of 15 to 29 mL/min) and used a fixed dose of delafloxacin 200 mg IV Q12h in these patients.
The study was conducted at 76 clinical sites in 15 countries including the US between 5/2/2014 and 1/29/2016. A total of 850 patients were enrolled and 734 patients completed the study.

Two clinical sites were selected for inspection: Dr. Hansen’s site was selected for inspection mainly because of high number of SAEs, with three SAEs in the study drug arm. Dr. Green’s site was selected for inspection mainly because of high enrollment, high site efficacy effect, and high number of SAEs, with four SAEs in study drug arm; in addition, the site shared the same address with Dr. Overcash’s site for Study 302.

According to the sponsor, in the primary efficacy analysis, the proportion of patients who were responders (≥20% reduction of erythema area) at 48 to 72 hours after initiation of study drug was similar in the 2 treatment groups in both Studies 302 and 303.
### III. RESULTS (by site):

<table>
<thead>
<tr>
<th>Site #/Name of CI/Address</th>
<th>Protocol # / # of Subjects Enrolled</th>
<th>Inspection Dates</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>840-327/ Hansen, Eric 730 Shore Road Somers Point, NJ 8244</td>
<td>RX-3341-303/34</td>
<td>12/12/2016 to 12/21/2016</td>
<td>VAI</td>
</tr>
<tr>
<td>840-002/ Overcash, Jeffrey 5565 Grossmont Center Drive, Building 3, Suite 525 La Mesa, CA 91942</td>
<td>RX-3341-302/154</td>
<td>1/13/2017 to 2/3/2017</td>
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<td>840-302/ Green, Sinikka 5565 Grossmont Center Drive, Building 3, Suite 525 La Mesa, CA 91942</td>
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<td>840-014/ Farley, Brett 1541 Florida Avenue, Suite 303 Modesto, CA 95350</td>
<td>RX-3341-302/27</td>
<td>1/4/2017 to 1/11/2017</td>
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</table>

Key to Compliance Classifications
NAI = No deviation from regulations.
VAI = Deviation(s) from regulations.
OAI = Significant deviations from regulations. Data unreliable.
*Pending = Preliminary classification based on information in Form FDA 483 or preliminary communication with the field; EIR has not been received from the field, or complete review of EIR is pending. Final classification occurs when the post-inspectional letter has been sent to the inspected entity.
Clinical Investigator Sites

1) Eric Hansen, D.O.
At this site for Protocol # RX-3341-303, 38 subjects were screened; 34 subjects were randomized; and 29 subjects completed the trial. There are no discrepancies between source document and FDA data listing regarding the reason of study discontinuation for the 5 subjects.

Informed consent forms (ICF) for all screened subjects were reviewed. Study records for all 17 subjects randomized to the investigational product were reviewed. Records reviewed included, but was not limited to, financial disclosure, training, protocol deviations, monitor and IRB communications, adverse events, laboratory reports, study visits, concomitant medications, and test article control. A comparison of source data for these 17 subjects randomized to the investigational drug to data listings was performed. Electronic Case Report Forms (eCRF) were reviewed when a discrepancy between the source document and data listing was observed.

An FDA Form 483, Inspectional Observations, was issued at the conclusion of the inspection for failure to conduct an investigation in accordance with the investigational plan. Observations included protocol deviations regarding two non-serious adverse events and prior antibacterial medication reporting:

1. Two adverse events (AEs) were not documented in the eCRF, facial eczema for Subject #3863 and pink and puffy IV injection site for Subject #3186.

2. A prior antibacterial treatment (Ancef) was not reported in the eCRF per protocol “up to 30 days before the first dose of study drug”: Subject 3059 (RAT) received the antibiotic Ancef prophylactically at 16 days prior to the first dose of study drug.

These observations were acknowledged by Dr. Hansen in his written response dated January 6, 2017, in which he indicated corrective actions were implemented to prevent the recurrence of the findings.

Notwithstanding the isolated deficiencies as noted above, the study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

2) Jeffrey Overcash, M.D.
At this site for Protocol # RX-3341-302, 164 subjects were screened; 154 subjects were enrolled; and 132 subjects completed the trial. There are no discrepancies between source document and FDA data listing regarding the reason of study discontinuation for the 22 subjects.

ICFs for all 164 screened subjects were reviewed. Infection site photographs used for calculation of primary efficacy endpoint and AE records were reviewed for all 154 subjects enrolled. Twenty two subject records were reviewed in depth.
An FDA Form 483 was issued at the conclusion of the inspection. Observations included:

A. Failure to prepare/maintain adequate case histories with respect to observations pertinent to investigation:

1) Documentation of AEs (34 out of 154 subjects): AE ending time or date was not entered into eCRF (e.g., for Subject 840-002-0070, the AE log record documents a worsening of a headache, mild, from 6/9/13 at 08:00 to 7/1/13; however, the stop date was not entered into the eCRF); severity of AEs in eCRF is not same as in the source documents (e.g., for Subject 840-002-0070, the AE log record documents worsening anxiety attack with a moderate severity while the eCRF documents a mild severity); missing AEs and its treatment in eCRF (e.g., for Subject 840-002-0172, the AE log source documents IV infiltration, mild on 8/8/13 and also on 8/12/13 with a start time of 21:29 and a stop date of 8/12/13; however, these AEs were not transcribed onto the eCRF).

2) Missing end date of concomitant medications (4 out of 22 subjects): e.g., for Subject 840-002-0069, oxycodone, 30 mg, from 6/4/13 to 6/9/13 in source document reports, but there was no end date in the eCRF.

3) Missing medical history (6 out of 22 subjects) in eCRF: e.g., for Subject 840-002-0026, medical history of mild myopia, and hypertension since 2003, hepatitis B/C since 1999, GERD (Gastroesophageal Reflux Disease) since 2010, occasional headaches since 2010, and depression/anxiety/schizophrenia since 2010 was not entered into the eCRF.

Reviewer’s comments: The above inspectional findings should not have been considered violations because the medical history described had onset over 2 years. According to the protocol “The medical history should include clinically significant medical or surgical history ongoing at baseline or with onset in the previous 2 years.”.

B. Investigation was not performed in accordance with investigational plan;

1) Protocol deviations per protocol’s digital photography of the infection area on Day 3 (12 hours apart): 9 out of 154 subjects did not have their two digital photos taken 12 hours apart on Day 3.

These observations were acknowledged by Dr. Overcash in his written response dated February 21, 2017, in which he indicated that corrective actions would be implemented to prevent the recurrence of the findings.

Multiple discrepancies between AE end times were noted between source documents and sponsor data listings. Although source documents and eCRFs reflected similar times and dates for AE start and date for AE resolution, the data listings did not reflect source and eCRF timing for resolution. For example, for Subject 840-002-0007, an AE of mild IV infiltration right antecubital stop date/time was 5/1/13 at 23:01 in source and eCRF, the sponsor’s data listing showed the stop date/time as 5/1/13 at 5:24 in the data listings. Based on preliminary information from the sponsor inspection, the sponsor is investigating this observation at this site or other site.

Reference ID: 4094909
Although regulatory violations were noted as described above, they are unlikely to significantly impact primary safety and efficacy analysis. The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

2) Sinikka Green, M.D.
At this site for Protocol # RX-3341-303, 61 subjects were screened, 55 subjects were randomized to the study, and 43 subjects completed the study. There are no discrepancies between source document and FDA data listing regarding the reason of study discontinuation for the 12 subjects.

ICFs for all 61 subjects screened were reviewed and demonstrated that all were signed prior to the initiation of any screening procedures. Records, including photographs for 55 subjects which were sent to the vendor for calculation of primary efficacy endpoint and AE records for all 55 enrolled subjects were reviewed, with 20 of the subject records reviewed in detail. Source data in the clinical investigator's records were verified with sponsor data listings submitted to the NDA.

Additional records reviewed included financial disclosure documents, protocol deviations, sponsor, monitor, and IRB communications, adverse events, and test article control.

Eight subjects were enrolled at both Dr. Green and Dr. Overcash’s sites subsequently, which did not violate the protocol eligibility criteria.

A Form FDA 483 was not issued at the conclusion of the inspection. This study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

3) Brett Farley, M.D.
At this site for Protocol # RX-3341-302, 43 patients were screened, and 27 patients were randomized to the study. There were 16 screen failures, and six subjects withdrew, terminated early, or were lost to follow-up.

Inspection included review of ICFs for the trial and an audit of the 27 randomized study subject binders. Records review included, but was not limited to, financial disclosure, protocol deviations, medical history, sponsor, monitor, and IRB communications, adverse events, digital photography of infection location, manual measurements, concomitant medications, local laboratory results, and test article control.

A Form FDA 483 was not issued at the conclusion of the inspection. This study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.
Sponsor Site

Melinta Therapeutics
The inspection audited Protocols RX-3341-302 and 303, and focused on the following clinical investigators: Drs. Hansen, Overcash, Green, and Farley. In addition, monitoring files of Dr. Vadym Schevchenko’s site (Site ID #784-063) in Ukraine were reviewed since it was the highest foreign enrollment site for Study 302 (n=26).

Based on an email communication with the ORA investigator, the sponsor appeared to maintain adequate oversight of the clinical trial. There was no evidence of under-reporting of adverse events at the sponsor site. The sponsor continues to investigate the cause of discrepancies in AE stop times in source documents/eCRF and the NDA data listings for at Dr. Overcash’s site. The stop dates for the adverse events appeared to be consistent between source/eCRF and data listings.

A Form FDA 483 was not issued at the conclusion of the inspection. The studies appear to have been conducted adequately by the sponsor, and the data at the selected clinical sites appears to be reliable as submitted by the sponsor and may be used in support of the respective indication.

{See appended electronic signature page}
Bei Yu, Ph.D.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE: {See appended electronic signature page}
Janice Pohlman, M.D., M.P.H.
Team Leader,
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE: {See appended electronic signature page}
Kassa Ayalew, M.D., M.P.H
Branch Chief
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CC:
Central Doc. Rm. / NDAs 208610&208611
DAIP /Division Director/
DAIP /Medical Team Leader/Thomas Smith
DAIP/Project Manager/Fariba Izadi
DAIP/MO/Caroline Jingo
OSI/DCCE/Division Director/Ni Khin
OSI/DCCE/Branch Chief/Kassa Ayalew
OSI/DCCE/Team Leader/Janice Pohlman
OSI/DCCE/GCP Reviewer/Bei Yu
OSI/GCP Program Analysts/Joseph Peacock/Yolanda Patague
OSI/Database PM/Dana Walters
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/s/

BEI YU  
05/08/2017

KASSA AYALEW  
05/08/2017

Reference ID: 4094909
Date: April 24, 2017

To: Sumathi Nambiar, MD, MPH
   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)

From: Twanda Scales, BSN, MSN/Ed.
   Patient Labeling Reviewer
   Division of Medical Policy Programs (DMPP)

Puja Shah, Pharm.D., RAC
   Regulatory Review Officer
   Office of Prescription Drug Promotion (OPDP)

Subject: Review of Patient Labeling: Medication Guide (MG)

Drug Name (established name): BAXDELA (delafloxacin)
Dosage Form and Route: tablets, for oral use
Application Type/Number: NDA 208610
1 INTRODUCTION
On October 18, 2016, Melinta Therapeutics submitted for the Agency’s review a new drug application (NDA) 208610, BAXDELA (delafloxacin) tablets, for oral use as an original 505(b)(1) application to support the indication for Acute Bacterial Skin and Skin Structure Infection (ABSSI).

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Anti-Infective Products (DAIP) on October 26, 2016, and October 25, 2016, respectively, for DMPP and OPDP to review the Applicant’s proposed Medication Guide (MG) for BAXDELA (delafloxacin) Tablets.

2 MATERIAL REVIEWED
- Draft BAXDELA (delafloxacin) Tablets, MG received on October 18, 2016, revised by the Review Division throughout the review cycle, and received by DMPP on April 13, 2017.
- Draft BAXDELA (delafloxacin) Tablets MG received on October 18, 2016, revised by the Review Division throughout the review cycle, and received by OPDP on April 13, 2017.
- Draft BAXDELA (delafloxacin) Tablets Prescribing Information (PI) received on October 18, 2016, revised by the Review Division throughout the review cycle, and received by DMPP on April 13, 2017.
- Draft BAXDELA (delafloxacin) Tablets Prescribing Information (PI) received on October 18, 2016, revised by the Review Division throughout the review cycle, and received by OPDP on April 13, 2017.
- Approved CIPRO (ciprofloxacin hydrochloride) comparator labeling dated July 26, 2016.
- Approved AVELOX (moxifloxacin hydrochloride) comparator labeling July 26, 2016.

3 REVIEW METHODS
In 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss. The ASCP and AFB recommended using fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss. We reformatted the MG document using the Arial font, size 10.

In our collaborative review of the MG we:
- simplified wording and clarified concepts where possible
- ensured that the MG is consistent with the Prescribing Information (PI)
• rearranged information due to conversion of the PI to Physicians Labeling Rule (PLR) format
• removed unnecessary or redundant information
• ensured that the MG is free of promotional language or suggested revisions to ensure that it is free of promotional language
• ensured that the MG meets the Regulations as specified in 21 CFR 208.20
• ensured that the MG meets the criteria as specified in FDA’s Guidance for Useful Written Consumer Medication Information (published July 2006)
• ensured that the MG is consistent with the approved comparator labeling where applicable.

4 CONCLUSIONS
The MG is acceptable with our recommended changes.

5 RECOMMENDATIONS
• Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
• Our collaborative review of the MG is appended to this memorandum. Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the MG.

Please let us know if you have any questions.
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/s/

TWANDA D SCALES
04/24/2017

PUJA J SHAH
04/24/2017

MARCIA B WILLIAMS
04/24/2017

LASHAWN M GRIFFITHS
04/25/2017
Memorandum

Date: April 24, 2017

To: Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective Products (DAIP)

From: Puja Shah, Pharm.D., RAC
Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

Subject: OPDP Labeling Consult Response
NDA 208610, 208611
BAXDELA™ (delafloxacin) tablets, for oral use
BAXDELA™ (delafloxacin) for injection, for intravenous use

As requested in DAIP's consult dated October 25, 2016, OPDP has reviewed the draft Package Insert (PI), Carton and Container Labeling (CCL), and Medication Guide (MG) for BAXDELA™ (delafloxacin) tablets, for oral use and BAXDELA™ (delafloxacin) for injection, for intravenous use (collectively referred to as Baxdela). OPDP’s comments are based on the substantially complete version of the labeling titled “Draft Label - PI delafloxacin.docx” which was accessed via http://sharepoint.fda.gov/orgs/CDER-OAP-DAIP/Active%20Documents/Draft%20Label%20-%20PI%20delafloxacin.docx on April 14, 2017.

Package Insert
Our comments on the draft PI are included directly on the attached copy of the labeling.

Carton and Container Labeling

OPDP reviewed the following proposed CCL accessed on April 24, 2017:

- Draft blister pack carton, bottle carton, and bottle label accessed via \CDSESUB1\evsprod\NDA208610\0041
- Draft vial carton and vial label accessed via \CDSESUB1\evsprod\NDA208611\0040

OPDP does not have any comments on the proposed CCL at this time.
Medication Guide

Our review of the MG will be conducted jointly with Division of Medical Policy Programs (DMPP) and filed under separate cover at a later date.

OPDP appreciates the opportunity to provide comments on these materials. If you have any questions or concerns, please contact Puja Shah at 240-402-5040 or puja.shah@fda.hhs.gov
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/s/

________________________________________
PUJA J SHAH
04/24/2017
MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum: March 31, 2017
Requesting Office or Division: Division of Anti-Infective Products (DAIP)
Application Type and Number: NDA 208610; NDA 208611
Product Name and Strength: Baxdela (Delafloxacin) Tablets, 450 mg;
Baxdela (Delafloxacin) for Injection, 300 mg/vial
Applicant/Sponsor Name: Melinta Therapeutics
Submission Date: March 30, 2017
OSE RCM #: 2016-2428; 2016-2429
DMEPA Primary Reviewer: Sevan Kolejian, PharmD
DMEPA Team Leader: Otto L. Townsend, Pharm D
1 PURPOSE OF MEMO
The Division of Anti-Infective Products (DAIP) requested that we review the container labels and carton labeling for Baxdela (Delafloxacin) tablets, submitted under NDA 208610 and Baxdela (Delafloxacin) for Injection submitted under NDA 208611 (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to DAIP’s request for information submitted to the Applicant via email communication dated, March 14, 2017 and recommendations that we made during a previous label and labeling review.a

2 CONCLUSION
The revised container label and carton labeling for Baxdela (Delafloxacin) tablets and Baxdela (Delafloxacin) for Injection are acceptable from a medication error perspective. We have no further recommendations at this time.

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/s/

SEVAN H KOLEJIAN
03/31/2017

OTTO L TOWNSEND
03/31/2017
LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review: February 3, 2017
Requesting Office or Division: The Division of Anti-Infective Products (DAIP)
Application Type and Number: NDA 208610; NDA 208611
Product Name and Strength: Baxdela (Delafloxacin) Tablets, 450 mg; Baxdela (Delafloxacin) for Injection, 300 mg/vial
Product Type: Single Ingredient
Rx or OTC: Rx
Applicant/Sponsor Name: Melinta Therapeutics
Submission Date: October 19, 2016
OSE RCM #: 2016-2428; 2016-2429
DMEPA Primary Reviewer: Sevan Kolejian, PharmD
DMEPA Team Leader: Vicky Borders-Hemphill, PharmD
1 REASON FOR REVIEW
Division of Anti-Infective Products (DAIP) requested that we review the container label, carton labeling, Medication Guide and prescribing information (PI) for Baxdela (Delafloxacin) tablets, under NDA 208610 and Baxdela (Delafloxacin) for Injection under NDA 208611 (See Appendix G) to determine if they are acceptable from a medication error perspective.

2 MATERIALS REVIEWED
We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

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<thead>
<tr>
<th>Material Reviewed</th>
<th>Appendix Section (for Methods and Results)</th>
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<td>Labels and Labeling</td>
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</tbody>
</table>

N/A=not applicable for this review
*We do not typically search FAERS for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED
We performed a risk assessment of the proposed container label, carton labeling, Medication Guide and Full Prescribing (FPI) Information for Baxdela (Delafloxacin) tablets and Baxdela (Delafloxacin) for injection to identify deficiencies that may lead to medication errors and for areas of improvement.

Full Prescribing Information (FPI)
Our review of the prescribing information (FPI) identified error-prone abbreviations, error prone trailing zeros that may pose confusion to the providers. We also noted that reconstitution volume of the diluent (10.5 ml) is different than the resulting solution volume (12 ml). We are concerned if the diluent volume of 10.5 mL will result in a sufficient volume to withdraw 12 mL from the vial and will result in a concentration of 25 mg/ml. We notified Office of Pharmaceutical Quality (OPQ) via email communication dated November 16, 2016 of the volume differences and defer to OPQ to make determination on the accuracy of resulting
reconstituted solution volume and concentration. In section 4.1, we provide additional recommendations to mitigate confusion and promote the safe use of this product.

**Container Label and Carton Labeling**

Our review of the container labels and carton labeling identified areas of improvement to increase clarity, prominence, and readability of important information. We note that the package type term appears on the container label and carton labeling for Baxdela (delafloxacin) for injection formulation. We defer to OPQ to make the final determination of the package type term for this product (see Section 4.2).

**4 CONCLUSION & RECOMMENDATIONS**

DMEPA concludes that the labels and labeling can be improved to increase clarity and prominence of important information to promote safe use of this product (See section 4.1 and section 4.2).

If you have further questions or need clarifications, please contact Janet Higgins, OSE Project Manager, at 240-402-0330.

**4.1 RECOMMENDATIONS FOR THE DIVISION**

We advise the following recommendations be implemented prior to approval:

**A. Full Prescribing Information (see Appendix F)**

1. Remove all dangerous abbreviations, including “IV” from the prescribing information. These abbreviations should not be used because they are frequently misinterpreted and can lead to mistakes that result in patient harm.\(^a\)\(^3\)
2. Remove the trailing zero (e.g. 12.0 mg) to avoid a ten-fold misinterpretation throughout the PI per Draft Guidance: Container and Carton, April 2013 (lines 469-472\(^b\)).
3. We note that the package type term appears throughout the labels and labeling. We defer to OPQ to make the final determination of the package type term for this product. Please ensure that the OPQ determined package type term is consistent throughout labels and labeling.

**B. In Dosage and Administration, section 2:**

1. Revise the statement to read “BAXDELA must be reconstituted and further diluted under aseptic conditions” for clarity.
2. In the 2\(^{nd}\) paragraph of section 2.3, relocate and revise the statement, to appear after the 1\(^{st}\) sentence of the 1\(^{st}\) paragraph for clarity of the

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sequence of steps for preparation. Revise the statement to read

3. We note that Dosage and administration section of the PI states using, using 10.5 mL of 5% Dextrose for Injection (D5W) or 0.9% Sodium Chloride Injection for each 300 mg vial and that the reconstituted vial contains 300 mg per 12 mL of Baxdela solution. Also noted that container label for the vial states that resulting solution will be 25 mg per ml concentration. We are concerned if the diluent volume of 10.5 mL will result in a sufficient volume to withdraw 12 mL from the vial and will result in a concentration of 25 mg/ml. We notified Office of Pharmaceutical Quality (OPQ) via email communication dated November 16, 2016 if the concentration and volume of the resulting solution is accurate and defer to OPQ to make the determine the accuracy of this statement.

C. How Supplied/Storage and Handling, Section 16.2:

1. Remove/ clarify abbreviations for clarity.

4.2 RECOMMENDATIONS FOR MELINTA THERAPEUTICS

We recommend the following be implemented prior to approval of NDA 208610 and NDA 208611:

I. BAXDELA (delafloxacin) for injection, vial; Container label and Carton labeling:

1. Revise statement on the primary display panel to read “Must be reconstituted and further diluted. For Intravenous Infusion Only.” We recommend this revision to minimize the risk of administering the drug as an intravenous bolus.

2. For clarity and to support correct amount of diluent to add to reconstitute delafloxacin for injection, revise the statement to read “Each 300 mg vial must be reconstituted with xx ml of D5W or 0.9% sodium chloride for injection and subsequently diluted only with D5W or 0.9% sodium chloride,” see package insert.”

II. BAXDELA (delafloxacin) tablets; 450 mg per tablet; Hospital Unit-Dose Carton Labeling:

1. Revise the quantity statement appearing on the Hospital Unit-Dose Carton Labeling to read “contains 20 tablets (2 blister cards of 10 tablet each)” for clarity of the total quantity.
APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Baxdela (delafloxacin) that Melinta Therapeutics submitted on October 19, 2016.

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APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis, along with postmarket medication error data, we reviewed the following Baxdela labels and labeling submitted by Melinta Therapeutics, Inc on October 19, 2016.

1. BAXDELA (delafloxacin) for injection; vial
   - Container label
   - Carton labeling

2. BAXDELA (delafloxacin) tablets; 450 mg per tablet
   - Container label and carton labeling for bottles of 20 tablets
   - Hospital unit-dose blister labels and carton labeling for hospital unit-dose carton labeling

3. Medication Guide

G.2 Label and Labeling Images

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/s/

SEVAN H KOLEJIAN
02/03/2017

BRENDA V BORDERS-HEMPHILL
02/03/2017
### Application Information

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<td>□ Animal Rule Confirmatory Study (SE10)</td>
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Proprietary Name: Baxdela - Conditionally acceptable  
Established/Proper Name: Delafloxacin  
Dosage Form: Tablets and Injection  
Strengths: 450 mg Tablet and 300 mg IV in Single use vial  

Applicant: Melinta Therapeutics  
Agent for Applicant (if applicable): N/A  
Date of Application: 10-18-16 submitted 10-19-16  
Date of Receipt: 10-19-16  
Date clock started after Unacceptable for Filing (UN): N/A  
PDUFA/BsUFA Goal Date: 06-19-17  
Filing Date: 12-18-16  
Action Goal Date (if different):  
Date of Filing Meeting: 11-16-16

Chemical Classification (original NDAs only):  
☑ Type 1- New Molecular Entity (NME); NME and New Combination  
☐ Type 2- New Active Ingredient; New Active Ingredient and New Dosage Form; New Active Ingredient and New Combination  
☐ Type 3- New Dosage Form; New Dosage Form and New Combination  
☐ Type 4- New Combination  
☐ Type 5- New Formulation or New Manufacturer  
☐ Type 7- Drug Already Marketed without Approved NDA  
☐ Type 8- Partial Rx to OTC Switch  
☐ Type 9-New Indication or Claim (will not be marketed as a separate NDA after approval)  
☐ Type 10-New Indication or Claim (will be marketed as a separate NDA after approval)  

Proposed indication(s)/Proposed change(s): ABSSSI

<table>
<thead>
<tr>
<th>Type of Original NDA:</th>
<th>Type of NDA Supplement:</th>
</tr>
</thead>
<tbody>
<tr>
<td>AND (if applicable)</td>
<td>505(b)(1)</td>
</tr>
<tr>
<td></td>
<td>505(b)(2)</td>
</tr>
</tbody>
</table>

If 505(b)(2)NDA/NDA Supplement: Draft the “505(b)(2) Assessment” review found at:  
**Type of BLA**

- [ ] 351(a)
- [ ] 351(k)

**Review Classification:**

**The application will be a priority review if:**

- [ ] A complete response to a pediatric Written Request (WR) was included (a partial response to a WR that is sufficient to change the labeling should also be a priority review – check with DPMH)
- [ ] The product is a Qualified Infectious Disease Product (QIDP)
- [ ] A Tropical Disease Priority Review Voucher was submitted
- [ ] A Pediatric Rare Disease Priority Review Voucher was submitted

**Resubmission after withdrawal?**

**Part 3 Combination Product?**

- [ ] Convenience kit/Co-package
- [ ] Pre-filled drug delivery device/system (syringe, patch, etc.)
- [ ] Pre-filled biologic delivery device/system (syringe, patch, etc.)
- [ ] Device coated/impregnated/combined with drug
- [ ] Device coated/impregnated/combined with biologic
- [ ] Separate products requiring cross-labeling
- [ ] Drug/Biologic
- [ ] Possible combination based on cross-labeling of separate products
- [ ] Other (drug/device/biological product)

**Fast Track Designation**

- [ ] Breakthrough Therapy Designation
  (set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager)
- [ ] Rolling Review
- [ ] Orphan Designation

**Collaborative Review Division (if OTC product):**

List referenced IND Number(s): IND 76096 & 62772

**Goal Dates/Product Names/Classification Properties**

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDUFA/BsUFA and Action Goal dates correct in the electronic archive?</td>
<td>✗</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
to the supporting IND(s) if not already entered into electronic archive.

<table>
<thead>
<tr>
<th>Application Integrity Policy</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the application affected by the Application Integrity Policy (AIP)? Check the AIP list at: <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a></td>
<td>☐</td>
<td>☒</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If yes, explain in comment column.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If affected by AIP, has OC been notified of the submission?</td>
<td>☐</td>
<td>☐</td>
<td>☒</td>
<td></td>
</tr>
<tr>
<td>If yes, date notified:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>User Fees</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is Form 3397 (User Fee Cover Sheet)/Form 3792 (Biosimilar User Fee Cover Sheet) included with authorized signature?</td>
<td>☒</td>
<td>☐</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>User Fee Status</th>
<th>Payment for this application (check daily email from <a href="mailto:UserFeeAR@fda.hhs.gov">UserFeeAR@fda.hhs.gov</a>):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Paid</td>
</tr>
<tr>
<td></td>
<td>Exempt (orphan, government)</td>
</tr>
<tr>
<td></td>
<td>Waived (e.g., small business, public health)</td>
</tr>
<tr>
<td></td>
<td>Not required</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>User Fee Bundling Policy</th>
<th>Payment of other user fees:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has the user fee bundling policy been appropriately applied? If no, or you are not sure, consult the User Fee Staff.</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>505(b)(2)</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>(NDAs/NDA Efficacy Supplements only)</td>
<td>☐</td>
<td>☒</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
cover letter, and annotated labeling). **If yes**, answer the bulleted questions below:

<table>
<thead>
<tr>
<th>Question</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?</td>
<td>☑️</td>
<td>☑️</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action is less than that of the reference listed drug (RLD)? [see 21 CFR 314.54(b)(1)].</td>
<td>☑️</td>
<td>☑️</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product’s active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug [see 21 CFR 314.54(b)(2)]?</td>
<td>☑️</td>
<td>☑️</td>
<td>x</td>
<td></td>
</tr>
</tbody>
</table>

**If you answered yes to any of the above bulleted questions, the application may be refused for filing under 21 CFR 314.101(d)(9). Contact the 505(b)(2) review staff in the Immediate Office of New Drugs for advice.**

<table>
<thead>
<tr>
<th>Question</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is there unexpired exclusivity on another listed drug product containing the same active moiety (e.g., 5-year, 3-year, orphan, or pediatric exclusivity)?</td>
<td>☑️</td>
<td>☑️</td>
<td>x</td>
<td></td>
</tr>
</tbody>
</table>

**Check the Electronic Orange Book at:**
http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm

**If yes, please list below:**

<table>
<thead>
<tr>
<th>Application No.</th>
<th>Drug Name</th>
<th>Exclusivity Code</th>
<th>Exclusivity Expiration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**If there is unexpired, 5-year exclusivity remaining on another listed drug product containing the same active moiety, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.)**

Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 314.108(b)(2).

Unexpired orphan or 3-year exclusivity may block the approval but not the submission of a 505(b)(2) application.

<table>
<thead>
<tr>
<th>Exclusivity</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does another product (same active moiety) have orphan exclusivity for the same indication? <strong>Check the Orphan Drug Designations and Approvals list at:</strong> <a href="http://www.accessdata.fda.gov/scripts/opdlisting/opd/index.cfm">http://www.accessdata.fda.gov/scripts/opdlisting/opd/index.cfm</a></td>
<td>☑️</td>
<td>☑️</td>
<td>x</td>
<td></td>
</tr>
</tbody>
</table>

**If another product has orphan exclusivity,** is the product considered to be the same product according to the orphan drug definition of sameness [see 21 CFR 316.3(b)(14)]?

**If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy**

<table>
<thead>
<tr>
<th>Exclusivity</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDAs/NDA efficacy supplements only: Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity?</td>
<td>☑️</td>
<td>☑️</td>
<td>☑️</td>
<td>10 years-5 years b/c of QIDP designation</td>
</tr>
</tbody>
</table>

**If yes,** # years requested: 10

**Note:** An applicant can receive exclusivity without requesting it:
therefore, requesting exclusivity is not required.

**NDAs only:** Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use?

<p>| | | |</p>
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</table>

**If yes,** did the applicant: (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)?

**If yes, contact the Orange Book Staff (CDER-Orange Book Staff).**

**BLAs only:** Has the applicant requested 12-year exclusivity under section 351(k)(7) of the PHS Act?

**If yes, notify Marlene Schultz-DePalo, CDER Purple Book Manager**

**Note:** Exclusivity requests may be made for an original BLA submitted under Section 351(a) of the PHS Act (i.e., a biological reference product). A request may be located in Module 1.3.5.3 and/or other sections of the BLA and may be included in a supplement (or other correspondence) if exclusivity has not been previously requested in the original 351(a) BLA. An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.

---

### Format and Content

**Do not check mixed submission if the only electronic component is the content of labeling (COL).**

<table>
<thead>
<tr>
<th></th>
<th>All paper (except for COL)</th>
<th>All electronic</th>
<th>Mixed (paper/electronic)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

**If mixed (paper/electronic) submission,** which parts of the application are submitted in electronic format?

<table>
<thead>
<tr>
<th></th>
<th>CTD</th>
<th>Non-CTD</th>
<th>Mixed (CTD/non-CTD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

**Overall Format/Content**

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>If electronic submission,</strong> does it follow the eCTD guidance?1</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>If not,</strong> explain (e.g., waiver granted).</td>
<td></td>
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</tr>
<tr>
<td><strong>Index:</strong> Does the submission contain an accurate comprehensive index?</td>
<td></td>
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</tr>
<tr>
<td><strong>Is the submission complete as required under 21 CFR 314.50 (NDAs/NDA efficacy supplements) or under 21 CFR 601.2 (BLAs/BLA efficacy supplements) including: legible</strong></td>
<td></td>
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</tr>
</tbody>
</table>

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If no, explain.

BLAs only: Companion application received if a shared or divided manufacturing arrangement?

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>☐</td>
<td>☑</td>
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<td></td>
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</tbody>
</table>

If yes, BLA #

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
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</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

Forms and Certifications

**Electronic** forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise, **paper** forms and certifications with hand-written signatures must be included.

**Forms** include: user fee cover sheet (3397/3792), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674); **Certifications** include: debarment certification, patent certification(s), field copy certification, and pediatric certification.

### Application Form

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is form FDA 356h included with authorized signature per 21 CFR 314.50(a)?</td>
<td>☑</td>
<td>☐</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**If foreign applicant, a U.S. agent must sign the form [see 21 CFR 314.50(a)(5)].**

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are all establishments and their registration numbers listed on the form/attached to the form?</td>
<td>☑</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
</tbody>
</table>

### Patent Information

(NDAs/NDA efficacy supplements only)

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is patent information submitted on form FDA 3542a per 21 CFR 314.53(c)?</td>
<td>☑</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
</tbody>
</table>

### Financial Disclosure

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature per 21 CFR 54.4(a)(1) and (3)?</td>
<td>☑</td>
<td>☐</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Forms must be signed by the APPLICANT, not an Agent [see 21 CFR 54.2(g)].**

**Note:** Financial disclosure is required for bioequivalence studies that are the basis for approval.

### Clinical Trials Database

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is form FDA 3674 included with authorized signature?</td>
<td>☑</td>
<td>☐</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**If yes, ensure that the application is also coded with the supporting document category, “Form 3674.”**

**If no, ensure that language requesting submission of the form is included in the acknowledgement letter sent to the applicant**
<table>
<thead>
<tr>
<th>Debarment Certification</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is a correctly worded Debarment Certification included with authorized signature?</td>
<td>☒</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Certification is not required for supplements if submitted in the original application. If foreign applicant, both the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications].*

*Note: Debarment Certification should use wording in FD&C Act Section 306(k)(1) i.e., “[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.” Applicant may not use wording such as, “To the best of my knowledge…”*

<table>
<thead>
<tr>
<th>Field Copy Certification (NDAs/NDA efficacy supplements only)</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>For paper submissions only: Is a Field Copy Certification (that it is a true copy of the CMC technical section) included?</td>
<td></td>
<td></td>
<td>☒</td>
<td></td>
</tr>
</tbody>
</table>

*Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)*

*If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.*

<table>
<thead>
<tr>
<th>Controlled Substance/Product with Abuse Potential</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>For NMEs: Is an Abuse Liability Assessment, including a proposal for scheduling, submitted per 21 CFR 314.50(d)(5)(vii)?</td>
<td></td>
<td></td>
<td>☒</td>
<td></td>
</tr>
</tbody>
</table>

*If yes, date consult sent to the Controlled Substance Staff:*

*For non-NMEs: Date of consult sent to Controlled Substance Staff:*

<table>
<thead>
<tr>
<th>Pediatrics</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>PREA</td>
<td>☒</td>
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</tbody>
</table>

*Does the application trigger PREA?*

*If yes, notify PeRC@fda.hhs.gov to schedule required PeRC meeting*[^2]

[^2]: [http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027829.htm](http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027829.htm)

Reference ID: 4020150

**Note:** NDAs/BLAs/efficacy supplements for new active ingredients (including new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.

<table>
<thead>
<tr>
<th>Table</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>If the application triggers PREA, is there an agreed Initial Pediatric Study Plan (iPSP)?</td>
<td>☒</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>If no, may be an RTF issue - contact DPMH for advice.</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>If required by the agreed iPSP, are the pediatric studies outlined in the agreed iPSP completed and included in the application?</td>
<td>☐</td>
<td>☒</td>
<td></td>
<td>Requested Ped Waiver</td>
</tr>
<tr>
<td>If no, may be an RTF issue - contact DPMH for advice.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BPCA:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is this submission a complete response to a pediatric Written Request?</td>
<td>☐</td>
<td>☒</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proprietary Name</td>
<td>YES</td>
<td>NO</td>
<td>NA</td>
<td>Comment</td>
</tr>
<tr>
<td>Is a proposed proprietary name submitted?</td>
<td>☒</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>If yes, ensure that the application is also coded with the supporting document category, “Proprietary Name/Request for Review.”</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>REMS</td>
<td>YES</td>
<td>NO</td>
<td>NA</td>
<td>Comment</td>
</tr>
<tr>
<td>Is a REMS submitted?</td>
<td>☐</td>
<td>☒</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If yes, send consult to OSE/DRISK and notify OC/OSI/DSC/PMSB via the CDER OSI RMP mailbox</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prescription Labeling</td>
<td>Not applicable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Check all types of labeling submitted.</td>
<td>☒</td>
<td></td>
<td></td>
<td>Package Insert (Prescribing Information)(PI)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Patient Package Insert (PPI)</td>
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<td></td>
<td>Instructions for Use (IFU)</td>
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<td></td>
<td>Medication Guide (MedGuide)</td>
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<td></td>
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<td></td>
<td>Carton labeling</td>
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<td>Immediate container labels</td>
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<td>Diluent labeling</td>
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<td></td>
<td></td>
<td></td>
<td>Other (specify) Blister Card</td>
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</tr>
<tr>
<td>Is Electronic Content of Labeling (COL) submitted in SPL format?</td>
<td>☒</td>
<td></td>
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</tr>
<tr>
<td>If no, request applicant to submit SPL before the filing date.</td>
<td></td>
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</tr>
<tr>
<td>Is the PI submitted in Physician Labeling Rule (PLR)</td>
<td>☒</td>
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</table>

[http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027837.htm](http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/OfficeofNonprescriptionProducts/PediatricandMaternalHealthStaff/ucm027837.htm)
### Format?

<table>
<thead>
<tr>
<th><strong>If PI not submitted in PLR format,</strong> was a waiver or deferral requested before the application was received or in the submission? <strong>If requested before application was submitted,</strong> what is the status of the request?</th>
<th>☐</th>
<th>☐</th>
<th>☑</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>If no waiver or deferral, request applicant to submit labeling in PLR format before the filing date.</strong></td>
<td>☑</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

### For applications submitted on or after June 30, 2015:

- **Is the PI submitted in Pregnancy and Lactation Labeling Rule (PLLR) format?**
  - ☑
  - ☐
  - ☐

- **Has a review of the available pregnancy, lactation, and females and males of reproductive potential data (if applicable) been included?**
  - ☑
  - ☐
  - ☐

### For applications submitted on or after June 30, 2015:

- **If PI not submitted in PLLR format,** was a waiver or deferral requested before the application was received or in the submission? **If requested before application was submitted,** what is the status of the request?
  - ☑
  - ☐
  - ☐

- **If no waiver or deferral, request applicant to submit labeling in PLLR format before the filing date.**
  - ☑
  - ☐
  - ☐

- **Has all labeling PI, patient labeling (PPI, MedGuide, IFU), carton and immediate container labeling]] been consulted to OPDP?**
  - ☑
  - ☐
  - ☐

- **Has PI and patient labeling (PPI, MedGuide, IFU) been consulted to OSE/DRISK? (send WORD version if available)**
  - ☑
  - ☐
  - ☐

- **Has all labeling PI, patient labeling (PPI, MedGuide, IFU) carton and immediate container labeling, PI, PPI been consulted/sent to OSE/DMEPA and appropriate CMC review office in OPQ (OBP or ONDP)?**
  - ☑
  - ☐
  - ☐

### OTC Labeling

- **Check all types of labeling submitted.**
  - ☑

<table>
<thead>
<tr>
<th>☐ Outer carton label</th>
<th>☐ Immediate container label</th>
<th>☐ Blister card</th>
<th>☐ Blister backing label</th>
<th>☐ Consumer Information Leaflet (CIL)</th>
<th>☐ Physician sample</th>
<th>☐ Consumer sample</th>
<th>☐ Other (specify)</th>
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</table>

**Is electronic content of labeling (COL) submitted?**

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
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<th>Comment</th>
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Reference ID: 4020150
If no, request in 74-day letter.

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<thead>
<tr>
<th align="left">Are annotated specifications submitted for all stock keeping units (SKUs)?</th>
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</table>

If no, request in 74-day letter.

<table>
<thead>
<tr>
<th align="left">If representative labeling is submitted, are all represented SKUs defined?</th>
<th></th>
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</table>

If no, request in 74-day letter.

<table>
<thead>
<tr>
<th align="left">All labeling/packaging sent to OSE/DMEPA?</th>
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</table>

**Other Consults**

<table>
<thead>
<tr>
<th align="left">Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team)</th>
<th></th>
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</tr>
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</table>

If yes, specify consult(s) and date(s) sent:

**Meeting Minutes/SPAs**

<table>
<thead>
<tr>
<th>End-of Phase 2 meeting(s)?</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
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</thead>
<tbody>
<tr>
<td>Date(s): 05-16-13 10-09-13 CMC</td>
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</table>

<table>
<thead>
<tr>
<th>Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)?</th>
<th>YES</th>
<th>NO</th>
<th>NA</th>
<th>Comment</th>
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<tbody>
<tr>
<td>Date(s): 03-15-16 Preliminary Comments</td>
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</table>

<table>
<thead>
<tr>
<th>Any Special Protocol Assessments (SPAs)?</th>
<th>YES</th>
<th>NO</th>
<th>Comment</th>
</tr>
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<tbody>
<tr>
<td>Date(s): 07-01-15</td>
<td></td>
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<td>ABSSSI</td>
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</tbody>
</table>
DATE: 10-24-16

BACKGROUND: Melinta is submitting NDA 208610, BAXDELA™ (delafloxacin) 450 mg Tablets and delafloxacin IV injections as original 505(b)(1) applications, to support the indication for Acute Bacterial Skin and Skin Structure Infection (ABSSSI).

IND 62772- delafloxacin Tab was submitted on 06-22-2001
IND 76096-delafloxacin IV submitted on 03-20-07

Fast Track was granted-12-18-12 for ABSSSI
QIDP was granted-09-08-12 for ABSSSI
SPA Agreement- 07-01-15 ABSSSI

REVIEW TEAM:

<table>
<thead>
<tr>
<th>Discipline/Organization</th>
<th>Names</th>
<th>Present at filing meeting? (Y or N)</th>
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</thead>
<tbody>
<tr>
<td>Regulatory Project Management</td>
<td>RPM: Fariba Izadi</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>CPMS/TL: Carmen DeBellas</td>
<td>Y</td>
</tr>
<tr>
<td>Cross-Discipline Team Leader (CDTL)</td>
<td>Tom Smith</td>
<td>Y</td>
</tr>
<tr>
<td>Division Director/Deputy for Safety</td>
<td>Sumathi Nambiar</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Toe Toerner</td>
<td>Y</td>
</tr>
<tr>
<td>Office Director/Deputy</td>
<td>Ed Cox</td>
<td>N</td>
</tr>
<tr>
<td>Clinical</td>
<td>Reviewer: Caroline Jjingo</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>TL: Tom Smith</td>
<td></td>
</tr>
<tr>
<td>Social Scientist Review (for OTC products)</td>
<td>Reviewer: NA</td>
<td></td>
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<td></td>
<td>TL: NA</td>
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<tr>
<td>OTC Labeling Review (for OTC products)</td>
<td>Reviewer: NA</td>
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<td></td>
<td>TL: NA</td>
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<tr>
<td>Clinical Microbiology (for antimicrobial products)</td>
<td>Reviewer: Jalal Sheikh</td>
<td>Y</td>
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<tr>
<td></td>
<td>TL: Tamara Feinberg</td>
<td>N</td>
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<tr>
<td>Clinical Pharmacology</td>
<td>Reviewer: Kunyi Wu</td>
<td>Y</td>
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<tr>
<td>Domain</td>
<td>Reviewer</td>
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<tr>
<td>Genomics</td>
<td>NA</td>
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<tr>
<td>Pharmacometrics</td>
<td>Luning (Ada) Zhuang, Jeff Florian</td>
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<tr>
<td>Biostatistics</td>
<td>Janelle Charles</td>
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<td>TL:</td>
<td>Karen Higgins, Dionne Price</td>
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<tr>
<td>Nonclinical (Pharmacology/Toxicology)</td>
<td>Wendy Schmidt</td>
<td></td>
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<tr>
<td>TL:</td>
<td>Terry Miller</td>
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<td>Statistics (carcinogenicity)</td>
<td>NA</td>
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<td>TL:</td>
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<tr>
<td>Product Quality (CMC) Review Team:</td>
<td>Balajee Shanmugam, Dorota Matecka</td>
<td></td>
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<tr>
<td></td>
<td>Luz Rodriguez</td>
<td></td>
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<tr>
<td>Drug Substance</td>
<td>Monica Cooper, Kasturi Srinivasachar</td>
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<td>Drug Product</td>
<td>Yushi Feng (Tab), Danuta Gromek Woods (IV)</td>
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<td>Process</td>
<td>Arwa El Hagrasy (IV), Upinder Atwal (IV), Steven Frisbee (Tab), Upinder Atwal (Tab)</td>
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<td>Microbiology</td>
<td>Steven Frisbee (Tab), Upinder Atwal (Tab), Jason God (IV), Neal Sweeney (IV)</td>
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<td>Facility</td>
<td>Aditi Thakur, Christina Capacci-Daniels</td>
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<td>Biopharmaceutics</td>
<td>Joan Zhao, Elsbeth Chikhale</td>
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<td>Immunogenicity</td>
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<td>Labeling (BLAs only)</td>
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<tr>
<td>Other (e.g., Branch Chiefs, EA Reviewer)</td>
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<tr>
<td>OMP/OMPI/DMPP (MedGuide, PPI, IFU)</td>
<td>Twanda Scales</td>
<td></td>
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<tr>
<td>TL:</td>
<td>Marcia Britt Williams</td>
<td></td>
</tr>
<tr>
<td>Task Description</td>
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<tr>
<td>---------------------------------------------------------------------------------</td>
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<td>OMP/OPDP (PI, PPI, MedGuide, IFU, carton and immediate container labeling)</td>
<td>Puja Shah</td>
<td>N</td>
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<tr>
<td></td>
<td>James Dvorsky</td>
<td>N</td>
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<tr>
<td>OSE/DMEPA (proprietary name, carton/container labeling)</td>
<td>Sevan Kolejian</td>
<td>Y</td>
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<tr>
<td></td>
<td>Vicky Hampton Borders</td>
<td>N</td>
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<tr>
<td>OSE/DPV</td>
<td>Jason Mihaela</td>
<td>N</td>
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<td>OSE/DRISK</td>
<td>Till Olickal</td>
<td>Y-Phone</td>
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<td>Kelly Kao</td>
<td>N</td>
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<td>OC/OSI/DSC/PMSB (REMS)</td>
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<td>Bioresearch Monitoring (OSI)</td>
<td>Bei Yu</td>
<td>N</td>
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<tr>
<td></td>
<td>Janice Pohlman</td>
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<tr>
<td>Controlled Substance Staff (CSS)</td>
<td>NA</td>
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<td></td>
<td>NA</td>
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<td>Other reviewers/disciplines</td>
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<td></td>
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<tr>
<td>• OSE</td>
<td>Natasha Pratt</td>
<td>N</td>
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<tr>
<td>Other attendees</td>
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<tr>
<td>John Lazor, Clinical Pharmacology, Director</td>
<td>Y</td>
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<tr>
<td>Amit Somani-Clinical Pharmacology Review</td>
<td>Y</td>
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<td>Abimbola Adebawale, Associate Director for labeling</td>
<td>Y</td>
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<td>Janet Higgins-OSE RPM</td>
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FILING MEETING DISCUSSION:

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<tr>
<td>• 505 b)(2) filing issues:</td>
<td></td>
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<tr>
<td>o Is the application for a duplicate of a listed drug and eligible</td>
<td></td>
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<tr>
<td>for approval under section 505(j) as an ANDA?</td>
<td></td>
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<tr>
<td>o Did the applicant provide a scientific “bridge” demonstrating the</td>
<td></td>
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<tr>
<td>relationship between the proposed product and the referenced</td>
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<tr>
<td>product(s)/published literature?</td>
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<tr>
<td>Describe the scientific bridge (e.g., information to demonstrate</td>
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<td>sufficient similarity between the proposed product and the listed</td>
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<td>drug(s) such as BA/BE studies or to justify reliance on information</td>
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<td>described in published literature):</td>
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<tr>
<td>Per reviewers, are all parts in English or English translation?</td>
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<td>If no, explain:</td>
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<td>Electronic Submission comments</td>
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<td>List comments:</td>
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<td></td>
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<td><strong>CLINICAL</strong></td>
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</tr>
<tr>
<td><strong>Comments:</strong> IRs will be sent prior to day 74.</td>
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<tr>
<td><strong>• Clinical study site(s) inspections(s) needed?</strong></td>
<td></td>
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<tr>
<td>If no, explain:</td>
<td>☒ YES</td>
<td></td>
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<td></td>
<td>☐ NO</td>
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<td><strong>• Advisory Committee Meeting needed?</strong></td>
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<td><strong>Comments:</strong></td>
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<td>If no, for an NME NDA or original BLA, include the reason. For example:</td>
<td></td>
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<tr>
<td>o this drug/biologic is not the first in its class</td>
<td></td>
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<td>o the clinical study design was acceptable</td>
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<tr>
<td>o the application did not raise significant safety or efficacy issues</td>
<td></td>
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<tr>
<td>o the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</td>
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<td>this drug/biologic is not the first in its class</td>
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<td>the clinical study design was acceptable</td>
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<td>the application did not raise significant safety or efficacy issues</td>
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<td>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</td>
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<tr>
<td><strong>• If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?</strong></td>
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<tr>
<td><strong>Comments:</strong></td>
<td>☒ Not Applicable</td>
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<tr>
<td></td>
<td>☐ YES</td>
<td></td>
</tr>
<tr>
<td></td>
<td>☐ NO</td>
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<tr>
<td><strong>CONTROLLED SUBSTANCE STAFF</strong></td>
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<tr>
<td><strong>• Abuse Liability/Potential</strong></td>
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<td><strong>Comments:</strong></td>
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<td></td>
<td>☐ FILE</td>
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</tr>
<tr>
<td></td>
<td>☐ REFUSE TO FILE</td>
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<td></td>
<td>☐ Review issues for 74-day letter</td>
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<tr>
<td><strong>CLINICAL MICROBIOLOGY</strong></td>
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<td><strong>Comments:</strong></td>
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<td></td>
<td>☐ REFUSE TO FILE</td>
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<tr>
<td>Category</td>
<td>Comments</td>
<td>Decision Options</td>
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<tr>
<td>----------------------------------------------------</td>
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<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>CLINICAL PHARMACOLOGY</strong></td>
<td>Will have IRs.</td>
<td>Not Applicable&lt;br&gt; FILE&lt;br&gt; REFUSE TO FILE&lt;br&gt; Review issues for 74-day letter</td>
</tr>
<tr>
<td>- Clinical pharmacology study site(s) inspections(s) needed?</td>
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<td>YES&lt;br&gt; NO</td>
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<tr>
<td><strong>BIOSTATISTICS</strong></td>
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<td>Not Applicable&lt;br&gt; FILE&lt;br&gt; REFUSE TO FILE&lt;br&gt; Review issues for 74-day letter</td>
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<tr>
<td><strong>NONCLINICAL (PHARMACOLOGY/TOXICOLOGY)</strong></td>
<td></td>
<td>Not Applicable&lt;br&gt; FILE&lt;br&gt; REFUSE TO FILE&lt;br&gt; Review issues for 74-day letter</td>
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<td><strong>PRODUCT QUALITY (CMC)</strong></td>
<td>will have IRs - will be sent by PQ PM.</td>
<td>Not Applicable&lt;br&gt; FILE&lt;br&gt; REFUSE TO FILE&lt;br&gt; Review issues for 74-day letter</td>
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<tr>
<td><strong>New Molecular Entity (NDAs only)</strong></td>
<td>Is the product an NME?</td>
<td>YES&lt;br&gt; NO</td>
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<tr>
<td><strong>Environmental Assessment</strong></td>
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<td>YES&lt;br&gt; NO</td>
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<tr>
<td>- Categorical exclusion for environmental assessment (EA) requested?</td>
<td></td>
<td>YES&lt;br&gt; NO</td>
</tr>
<tr>
<td>If no, was a complete EA submitted?</td>
<td></td>
<td>YES&lt;br&gt; NO</td>
</tr>
<tr>
<td><strong>Facility Inspection</strong></td>
<td>Establishment(s) ready for inspection?</td>
<td>Not Applicable&lt;br&gt; YES&lt;br&gt; NO</td>
</tr>
<tr>
<td><strong>Comments:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Facility/Microbiology Review (BLAs only)</td>
<td>Comments:</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>------------</td>
<td></td>
</tr>
<tr>
<td></td>
<td>☒ Not Applicable</td>
<td></td>
</tr>
<tr>
<td></td>
<td>FILE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>REFUSE TO FILE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>☐ Review issues for 74-day letter</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CMC Labeling Review (BLAs only)</th>
<th>Comments:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>☐ Review issues for 74-day letter</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs)</th>
<th>Comments:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Were there agreements made at the application’s pre-submission meeting (and documented in the minutes) regarding certain late submission components that could be submitted within 30 days after receipt of the original application?</td>
<td>☒ YES</td>
</tr>
<tr>
<td>If so, were the late submission components all submitted within 30 days?</td>
<td>☒ YES</td>
</tr>
<tr>
<td></td>
<td>☒ NO</td>
</tr>
<tr>
<td>What late submission components, if any, arrived after 30 days?</td>
<td>NA</td>
</tr>
<tr>
<td>Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?</td>
<td>☒ YES</td>
</tr>
<tr>
<td>Is a comprehensive and readily located list of all clinical sites included or referenced in the application?</td>
<td>☒ YES</td>
</tr>
<tr>
<td>Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?</td>
<td>☒ YES</td>
</tr>
</tbody>
</table>
**REGULATORY PROJECT MANAGEMENT**

**Signatory Authority:** Edward Cox, MD

**Date of Mid-Cycle Meeting** (for NME NDAs/BLAs in “the Program” PDUFA V): 01-25-17

**21st Century Review Milestones (see attached)** (listing review milestones in this document is optional):

**Comments:**

### REGULATORY CONCLUSIONS/DEFICIENCIES

- The application, on its face, appears to be suitable for filing.

  **Review Issues:**
  - No review issues have been identified for the 74-day letter. (IRs will be sent prior to 74-day letter)
  - Review issues have been identified for the 74-day letter.

  **Review Classification:**
  - Standard Review
  - Priority Review

### ACTION ITEMS

- Ensure that any updates to the review priority (S or P) and classifications/properties are entered into the electronic archive (e.g., chemical classification, combination product classification, orphan drug).

- If RTF, notify everyone who already received a consult request, OSE PM, and RBPM

- If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.

- If priority review, notify applicant in writing by day 60 (see CST for choices)

- Send review issues/no review issues by day 74

- Conduct a PLR format labeling review and include labeling issues in the 74-day letter

- Update the PDUFA V DARRTS page (for applications in the Program)

- Other

Annual review of template by OND ADRAs completed: April 2016
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
11/29/2016

CARMEN L DEBELLAS
11/29/2016