CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

208610Orig1s000
208611Orig1s000

Trade Name:	Baxdela Tablets, 450 mg; Baxdela for Injection, 300 mg/vial
Generic or Proper Name:	Delafloxacin Tablets; Delafloxacin for Injection
Sponsor:	Melinta Therapeutics
Approval Date:	June 19, 2017
Indication:	Indicated in adults for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by designated susceptible bacteria.

CENTER FOR DRUG EVALUATION AND RESEARCH

208610Orig1s000
208611Orig1s000

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208610Orig1s000
208611Orig1s000

APPROVAL LETTER

NDA 208610
NDA 208611

NDA APPROVAL

Melinta Therapeutics, Inc.
Attention: Peter DiRoma
Vice President Regulatory Affairs and Quality Assurance
300 Tri-State International, Suite 272
Lincolnshire, IL 60069

Dear Mr. DiRoma:

Please refer to your New Drug Applications (NDAs) dated October 18, 2016, received October 19, 2016, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

NDA	Drug	Strength and Dosage Form
208610	Baxdela (delafloxacin)	450 mg Tablets
208611	Baxdela (delafloxacin)	300 mg Injection

These new drug applications provide for the use of Baxdela (delafloxacin) Tablets and Baxdela (delafloxacin) Injection for treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSI).

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

WAIVER OF HIGHLIGHTS SECTION

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert, , Medication

Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3).* For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 208610 and 208611**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for Baxdela was not referred to an FDA advisory committee because the application did not raise significant safety or efficacy issues that were unexpected for a drug of this class.

REQUIRED PEDIATRIC ASSESSMENTS

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

We are waiving the pediatric study(ies) requirement for these applications because risk-benefit considerations do not support the use of Baxdela for ABSSSI in this population. Fluoroquinolones cause arthropathy in juvenile animals.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess a known serious risk of development of resistance to Baxdela (delafloxacin) in organisms specific to the ABSSSI

indication in the label, or to identify an unexpected serious risk of embryo-fetal toxicity due to exposure to Baxdela (delafloxacin). Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore based on appropriate scientific data FDA has determined that you are required to conduct the following:

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 ABSSSI indication in the label.

The timetable you submitted on May 31, 2017, states that you will conduct this study according to the following schedule:

Final protocol submission:	09/ 2017
First interim report:	07/ 2018
Second interim report:	07/ 2019
Third interim report:	07/ 2020
Fourth interim report:	07/ 2021
Fifth interim report:	07/ 2022
Study completion date:	09/ 2022
Final report submission date:	12/ 2022

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 (SBECD) to assess the distribution of the drug substance to the reproductive tract and developing fetus.

The timetable you submitted on May 31, 2017, states that you will conduct this study according to the following schedule.

Final Protocol Submission:	10/2017
Study Completion:	03/2018
Final Report Submission:	06/2018

3220-3: If the results of the tissue distribution studies from PMR 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.

The timetable you submitted on May 31, 2017, states that you will conduct this study according to the following schedule.

Final Protocol Submission:	07/2018
Study Completion:	01/2019
Final Report Submission:	04/2019

Submit clinical protocol(s) to your IND 62772 (Tablet) and IND 76096 (IV) with a cross-reference letter to these NDAs. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final reports to your NDAs. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **Required Postmarketing Protocol Under 505(o), Required Postmarketing Final Report Under 505(o), Required Postmarketing Correspondence Under 505(o).**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii) . We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments for NDA **208610**:

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

The timetable you submitted on June 06, 2017, states that you will conduct this study according to the following schedule.

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

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

The timetable you submitted on June 06, 2017, states that you will conduct this study according to the following schedule.

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

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.

The timetable you submitted on June 06, 2017, states that you will conduct this study according to the following schedule.

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

We remind you of your postmarketing commitments for NDA **208611**:

3220-7: 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 at (b) (4)

The timetable you submitted on June 07, 2017, states that you will conduct this study according to the following schedule.

Study Completion:	08/01/2017
Final Report Submission:	09/01/2017

3220-8: Provide PV data to support a more suitable In-Process Control (IPC) limit at (b) (4)% of (b) (4) as a CBE-30 in lieu of the proposed specification ((b) (4)% of target, (b) (4) mg/mL) in NDA 208611.

The timetable you submitted on June 07, 2017, states that you will conduct this study according to the following schedule.

Study Completion:	08/01/2017
Final Report Submission:	09/01/2017

Submit clinical protocols to your IND 62772 (Tablet) and IND 76096 (IV) for these products. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission

dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **"Postmarketing Commitment Protocol," "Postmarketing Commitment Final Report," or "Postmarketing Commitment Correspondence."**

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert, Medication Guide, and patient PI (as applicable) to:

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

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biologics qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

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

Sincerely,

{See appended electronic signature page}

John Farley, MD, MPH
Deputy Director
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosure(s):
Content of Labeling
Carton and Container Labeling

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

/s/

JOHN J FARLEY
06/19/2017