NDA 208610/S-007
NDA 208611/S-006

SUPPLEMENT APPROVAL

Melinta Therapeutics, Inc.
Attention: Starr Shangle
Senior Director, Regulatory Affairs
300 Tri-State International, Suite 272
Lincolnshire, IL 60069

Dear Ms. Shangle:

Please refer to your supplemental new drug applications (sNDAs) dated April 24, 2019, received April 24, 2019, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for the following:

NDA 208610/S-007 Baxdela (delafloxacin) 450 mg tablets
NDA 208611/S-006 Baxdela (delafloxacin) 300 mg injection

These Prior Approval supplemental new drug applications provide for the use of Baxdela (delafloxacin) 450 mg tablets and Baxdela (delafloxacin) 300 mg injection for the treatment of Community-Acquired Bacterial Pneumonia (CABP) in adults due to designated susceptible bacteria.

APPROVAL & LABELING

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.

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 FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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*.[2]

The SPL will be accessible from publicly available labeling repositories.

Also, within 14 days, amend all pending supplemental applications that include labeling changes for these NDAs, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in these supplemental applications, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the requirement for pediatric studies for these applications for patients 0 to < 2 months of age because studies in CABP in this population would be impossible or highly impracticable. This is because CABP is infrequent in this age group.

We are deferring submission of your pediatric studies for ages 2 months to less than 18 years for these applications because these products are ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the FDCA. These required studies are listed below.

3727-1 Conduct a randomized 2-sequence, 2-period, crossover study in fasted healthy adults to determine the relative bioavailability of the delafloxacin tablet and an oral pediatric formulation of delafloxacin.

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

The timetable you submitted on October 21, 2019, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	01/2020
Final Protocol Submission:	03/2020
Study/Trial Completion:	04/2020
Final Report Submission:	10/2020

3727- 2 Conduct an open-label, multi-center study evaluating the PK and safety of delafloxacin as a single IV dose, an oral tablet or an oral pediatric formulation administered as add-on therapy to standard of care (SOC) antimicrobial agents in patients 2 months to <18 years of age with suspected or confirmed bacterial infections due to delafloxacin susceptible organisms.

The timetable you submitted on October 21, 2019, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	07/2020
Final Protocol Submission:	10/2020
Study/Trial Completion:	12/2022
Final Report Submission:	06/2023

3727-3 Conduct a randomized open label, active-controlled, evaluator-blinded safety and PK trial of delafloxacin in patients 2 months to <18 years of age with suspected or confirmed CABP.

The timetable you submitted on October 21, 2019, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	02/2023
Final Protocol Submission:	06/2023
Study/Trial Completion:	02/2026
Final Report Submission:	09/2026

Submit the protocols to your INDs 62772 and 76096, with a cross-reference letter to these NDAs.

Reports of these required pediatric postmarketing studies must be submitted as new drug applications (NDAs) or as supplements to your approved NDAs with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

POSTMARKETING REQUIREMENT 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 identify the serious risk of development of resistance to BAXDELA in microorganisms specific to the indications in the label.

We note that PMR 3220-1, listed in the June 19, 2017, NDA approval letter was specific to the acute bacterial skin and skin structure infections (ABSSSI) indication. We also note that you have submitted the final protocol and the first and second interim reports for this study. PMR 3220-1 is therefore replaced with PMR 3727-4 that includes both the ABSSSI and CABP indications.

Furthermore, the new pharmacovigilance system that FDA is required to establish under 505(k)(3) of the FDCA will not be sufficient to assess this serious risk. Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

3727-4 Conduct a United States surveillance study to determine if resistance to delafloxacin has developed in organisms specific to the indications in the label.

The timetable you submitted on October 21, 2019, states that you will conduct this study according to the following schedule:

First interim report	Submitted
Second interim report	Submitted
Third interim report:	07/ 2020
Fourth interim report:	07/ 2021
Fifth interim report:	07/ 2022
Sixth interim report:	07/ 2023
Seventh interim report:	07/ 2024
Study completion date:	09/ 2024
Final report submission date:	12/ 2024

Submit your interim reports and final report to your NDAs. Prominently identify the submissions with the following wording in bold capital letters at the top of the first page of each submission, as appropriate: **Required Postmarketing Correspondence Under 505(o), Required Postmarketing Final Report 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 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 the FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the Prescribing Information to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
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 *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5] For more information

[3] When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see FDA.gov.[6]

REPORTING REQUIREMENTS

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

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

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide

[6] http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm

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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

SUMATHI NAMBIAR
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