NDA 215457/S-001

SUPPLEMENT APPROVAL
RELEASE FROM POSTMARKETING REQUIREMENTS

Kaleo, Inc.
111 Virginia Street, Suite 300
Richmond, VA 23219

Attention: Breanne N. Gjurich, PhD
Manager, Regulatory Affairs

Dear Dr. Gjurich:

Please refer to your supplemental new drug application (sNDA) dated and received, October 6, 2022, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Naloxone hydrochloride injection auto-injector.

This "Changes Being Effected" supplement provides for reduction of the (b) (4) acceptance criteria from NMT (b) (4)% to NMT (b) (4)% for release and stability specifications to support release of postmarketing requirements (PMRs) 4228-3, 4228-4, and 4228-5 associated with the qualification of (b) (4), which were issued in our approval letter dated February 28, 2022.

APPROVAL

We have completed our review of this supplemental new drug application, and it is approved.

RELEASE OF POSTMARKETING REQUIREMENTS

We have reviewed your submission dated October 6, 2022, related to the following PMRs listed in our February 28, 2022, approval letter:

4228-3 Conduct a GLP in vitro genetic toxicology Ames assay testing the potential for the naloxone degradant, (b) (4), to induce point mutations.

Draft Protocol Submission:	04/2022
Final Protocol Submission:	06/2022
Study Completion:	09/2022
Final Report Submission:	01/2023

4228-4 Conduct a GLP in vitro genetic toxicology study characterizing the potential of the naloxone degradant, [redacted] (b) (4) to induce chromosomal damage.

Draft Protocol Submission:	04/2022
Final Protocol Submission:	06/2022
Study Completion:	09/2022
Final Report Submission:	01/2023

4228-5 Conduct a GLP repeat-dose toxicology study of at least 14 days duration in a single species to characterize the toxicologic potential of the naloxone degradant, [redacted] (b) (4)

Draft Protocol Submission:	08/2022
Final Protocol Submission:	11/2022
Study Completion:	07/2023
Final Report Submission:	11/2023

We have reviewed your submission and have determined that you are released from the above requirements as they are no longer needed because the reduction of the drug product specification for [redacted] (b) (4) to NMT [redacted] (b) (4)% is within the qualification threshold permitted in ICH Q3B and therefore further study is not required.

We remind you that there are postmarketing requirements listed in our February 28, 2022, approval letter which are still open.

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

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

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.[1]

If you have any questions, contact Kimberly Compton, RPh, RAC, Senior Regulatory Project Manager, at 301-796-1191.

Sincerely,

{See appended electronic signature page}

Celia J Winchell, MD
Associate Director for Therapeutic Review,
Addiction Medicine
Division of Anesthesiology, Addiction
Medicine, and Pain Medicine
Office of Neuroscience
Center for Drug Evaluation and Research

[1] https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products

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/s/

CELIA J WINCHELL
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