NDA 017058/S-027

SUPPLEMENT APPROVAL

Hikma Pharmaceuticals USA Inc.
1809 Wilson Road
Columbus, OH 43228

Attention: Chrysoula Koukoutsis
Associate Director, Drug Regulatory Affairs

Dear Ms. Koukoutsis:

Please refer to your supplemental new drug application (sNDA) dated and received August 10, 2020, and your amendment, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Diskets (methadone hydrochloride) tablets.

We also refer to our letter dated July 23, 2020, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for opioid analgesic products used in the outpatient setting and products approved for medication-based treatment of opioid use disorder. This information pertains to the risk of fatal overdose to patients and their close contacts who may be at elevated risk of opioid overdose, and that increasing access to FDA-approved naloxone for some patients at elevated risk may help reduce the risk of fatal opioid overdose.

We also refer to our letter dated February 17, 2021, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for methadone-containing products. This information pertains to the risk of risks to the fetus and newborn related to methadone exposure, congenital oculomotor disorders, rhabdomyolysis, acute toxic leukoencephalopathy, and ototoxicity.

This supplemental new drug application, as amended, provides for revisions to the labeling for methadone-containing products, and is consistent with our July 23, 2020, and February 17, 2021, letters.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

We note that your March 16, 2021, submission includes final printed labeling (FPL) for your Prescribing Information. We have not reviewed this FPL. You are responsible for

assuring that the wording in this FPL is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

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, 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.

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 this NDA, 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 this supplemental application, 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).

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

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[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[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.
[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

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]

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

If you have any questions, call LCDR Jessica Voqui, PharmD, MS, Safety Regulatory Project Manager, at 301-796-2915.

Sincerely,

{See appended electronic signature page}

LCDR Mark A. Liberatore, PharmD, RAC
Deputy Director for Safety
Division of Anesthesiology, Addiction Medicine, and Pain Medicine
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURE:

- Content of Labeling
    - Prescribing Information

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

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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/

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