NDA 022276/S-025

APPROVAL LETTER

Hikma International Pharmaceuticals LLC
c/o Hikma Pharmaceuticals USA Inc
Attention: J Barton Kalis
Sr. Director, Regulatory Affairs
2 Esterbrook Lane
Cherry Hill, NJ 08003

Dear Mr. Kalis:

Please refer to your Supplemental New Drug Application (sNDA) dated and received February 12, 2024, and your amendments, pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for nicardipine hydrochloride injection.

This "Changes Being Effected" supplemental new drug application provides for:
The response for CBE-0 Labeling supplement request by Dr. Gurpreet Gill-Sangha, PhD, Branch Chief, Division of Post Marketing Activities on August 1, 2022. Following IR was sent for CBE-0 supplement request on 08/01/2022.

During a recent labeling review for Nicardipine Hydrochloride injection, 25 mg/10 mL (2.5 mg/mL), 20mg/200 mL (0.1 mg/mL) and 40 mg/200 mL (0.2 mg/mL), NDA-022276, we noted that there is discrepancy in composition mentioned in section 3.2.P.1 (S-20, SEQ 59, received on 7/13/2021) and the package insert. We also noted some other deficiencies in PI. We recommend that you make following revisions accordingly in current approved Prescribing Information (PI), bag and wrap and submit the labeling changes to the Agency through CBE 0 labeling supplement. The following recommendations are for the 20mg/200 mL (0.1 mg/mL) and 40 mg/200 mL (0.2 mg/mL) strengths only:

1. We note that in section 3.2.P.1, the composition Table 4 (S-20, SEQ 59, received on 7/13/2021) lists sodium chloride (b) (4) mg/mL whereas the package inserts, composition table 3 (S-20, SEQ 59, received on 7/13/2021), batch formula, and executed batch record (EBR) list sodium chloride 9 mg/mL for both the 0.1 mg/mL and 0.2 mg/mL strengths. The quantity of sodium chloride in the composition table (Table 4) does not align with the package insert. Please clarify this discrepancy.
2. Add an appropriate package type term in alignment with the container labels (e.g. Single Dose Container) in DOSAGE FORMS AND STRENGTHS (HIGHLIGHTS and Section 3); Section 2.2 Inspection and Preparation; and Section 11 DESCRIPTION, per USP General Chapter <659> Packaging and Storage Requirements, and Guidance Selection of the Appropriate Package Type Terms and recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018).

3. Add a discard statement in section 2.2 Inspection and Preparation in alignment with the container labels (e.g., Discard Unused Portion) and Guidance Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018).
4. We also note that the bag and overwrap for the 20mg/200 mL (0.1 mg/mL) and 40 mg/200 mL (0.2 mg/mL) strengths states "STORE IN CARTON UNTIL READY TO USE." Additionally, in supplement-008 (received on 3/29/2013, approved on 4/07/2016) section 3.2.P.7 Container Closure System states the product is packaged in cartons containing 10 bags (see excerpts below). Confirm if there is a carton for bags and if the carton for bags has a label then submit the label for review.
5. Revise the CAUTION statement on injection Bag and Over wrap from "CAUTIONS: Check for minute leaks by squeezing bag firmly. Do not use unless……" to "CAUTIONS: Check for minute leaks. Do not use unless……".

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is 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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the patient package insert) 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.

The SPL will be accessible via 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 MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes, and annotate each change. To facilitate review of your submission, 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).

CARTON AND CONTAINER LABELS

Submit final printed carton and container labels that are identical to carton and container labels submitted on August 9, 2024, 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 *Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Product Correspondence – Final Printed Carton and Container Labels for approved NDA 022276/S-025.**" Approval of this submission by FDA is not required before the labeling is used.

We remind you that you must comply with reporting requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Grafton Adams at grafton.adams@fda.hhs.gov

Sincerely,

{See appended electronic signature page}

Gurpreet Gill-Sangha, Ph.D.
Supervisor
Division of Product Quality Assessment II
Office of Product Quality Assessment I
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research

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

Gurpreet
Gill Sangha

Digitally signed by Gurpreet Gill Sangha
Date: 8/16/2024 07:44:15AM
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