Regulatory Affairs
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RESPONSE TO PREA NON-COMPLIANCE LETTER
DEFERRAL EXTENSION REQUESTED

May 14, 2025

CDER Central Document Room:
FDA/Center for Drug Evaluation and Research (CDER)
Central Document Room (CDR)
5901-B Ammendale Road
Beltsville, MD 20705-1266

RE: NDA 203826
Phenylephrine Hydrochloride Injection, USP
10 mg/mL, 1 mL vials

Dear Colleague:

Reference is made to Hikma Pharmaceuticals USA Inc.'s approved New Drug Application for Phenylephrine Hydrochloride Injection USP, 10 mg/mL, 1 mL vials, marketed under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act.

Reference is also made to the postmarketing requirement (PMR 1991-1) of the Pediatric Research Equity Act (PREA) for this application deferred until December 31, 2024. Additional reference is made to the Agency's Notification of Non-Compliance with PREA dated April 3, 2025. Further reference is made to the Clinical Pediatric Study Protocol 1420-RDP-009 Amendment 2 (Version 3.0), submitted February 25, 2016 to IND 109977. The protocol states:

- *"A sufficient number of subjects will be enrolled in this study in order to assure that 100 subjects will experience a decrease in BP that requires treatment and will receive PHI (50 subjects via infusion and 50 subjects as a bolus.)"*

During the course of this study, seven sites have closed due to lack of enrollment and at present three sites remain. However, of the remaining sites, two sites are currently recruiting study subjects throughout the United States, and the other site is in the process of withdrawing from the study. To date a total of 68 subjects have been dosed and completed the study for Cohorts 1 through 4. Cohort 5 is open and currently enrolling subjects; to date a total of 9 subjects have been dosed and completed the study.

Due to slow enrollment and challenges with the study, it was not possible to enroll the number of study subjects required to comply with the goal date of study completion by June 30, 2024 and final report submission by December 31, 2024. Enclosed in Module 1.9.2 is a summary of current enrollment.

Given the inherent challenges to enrollment in this pediatric study and based on the enrollment rate to date, our projection for study completion is December 2026. Therefore, we wish to request deferral extensions as follows:

- Study/Trial Completion: December 31, 2026
- Final Report Submission: June 30, 2027

To facilitate the completion of this study, Hikma has contracted a third-party consultant to perform a population PK analysis using the study data from Cohorts 1 through 4. The consultant is performing this analysis and applying the same principles to make assumptions for the remainder of the data through Cohorts 5 and 6 to extend to a general population assumption for pediatric safety and efficacy. Cohort 5 continues to enroll subjects while the data from Cohorts 1 through 4 is being analyzed. This third-party contract work has been in process since October 2024 and we are expecting the analysis results from the consultant by May 2025.

If the analysis of the data demonstrates pediatric safety and efficacy through Cohort 4, Hikma will be asking the FDA for approval to stop enrollment and discontinue the study. Cohort 5 will continue to enroll until we file the request for discontinuation and receive a response from the FDA. We are targeting submitting our data package with our request in June 2025.

This amendment is being submitted via the Electronic Submissions Gateway (ESG).

If you have any questions concerning this submission, please contact the undersigned or J. Barton Kalis, AVP, Regulatory Affairs at 856-489-2247 (direct), 856-489-2100 (facsimile) or jkalis@hikma.com (email).

Sincerely,

Angela M. Zimarowski
Digitally signed by Angela M. Zimarowski
Date: 2025.05.14 14:00:12 -04'00'

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