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September 14, 2023

Food and Drug Administration
Division of Anesthesia, Analgesia, and Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Beltsville, MD 20705-1266

Attention: Cooma Asonye, Regulatory Project Manager

NDA 022195
Morphine Sulfate Oral Solution
NDA 022207
Morphine Sulfate Tablets

RESPONSE TO PREA NON-COMPLIANCE LETTER

Dear Cooma Asonye,

Reference is made to the New Drug Applications (NDA) referenced above and to the the June 14, 2023 Notification of Non-Compliance with PREA received from the FDA.

Based on the data provide in the attached **Request for Waiver of Pediatric Studies**, Hikma Pharmaceuticals USA Inc. (Hikma) is again requesting the Agency's consideration of a partial waiver under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c) for the study of oral morphine sulfate solution and morphine sulfate tablets in pediatric patients aged 0 to <2 years.

On 11 June 2021, Hikma submitted a request for a partial waiver for the study of morphine sulfate oral solution and morphine sulfate tablets in pediatric patients aged 0 (birth) to <2 years, citing the criteria supporting the waiver request as follows (in accordance with the Food and Drug Administration (FDA) Draft Guidance for Industry, "How to Comply with the Pediatric Research Equity Act", dated September 2005):

> Necessary studies are highly impracticable (because, for example, the number of patients is so few, or the patients are geographically dispersed) (section 505B(a)(4)(A)(i) of the Act.

At that time, the Agency denied the waiver request pending the outcome of a public workshop in October 2021, titled, "Analgesic Clinical Trial Designs, Extrapolation, and Endpoints in Patients from Birth to Less than Two Years of Age." The Agency recommended that Hikma assess the outcome of this meeting and contact the Agency following the October workshop.

As recommended by the Agency, Hikma assessed the outcome of the public workshop and summarized input from participants that overwhelmingly support Hikma's requested PREA waiver in this age range (birth to 2 years).

Furthermore, Hikma plans to conduct a feasibility assessment to demonstrate that a study in patients aged 0 to <2 years is highly impracticable or potentially impossible based on the foreseeable challenge in enrollment given the current clinical practice for this demographic.

In summary, Hikma requests that a waiver of Postmarketing Requirement (PMR) 204-4 issued with the New Drug Application (NDA) approval on 17 March 2008 be granted. Additionally, at this time a final protocol has not been submitted due to no clinical sites wish to perform the pediatric study (0-2 year old).

This amendment is an electronic submission and is formatted in accordance with the Common Technical Document (CTD) Guidance and related ICH and Agency Guidelines. We certify that this amendment is virus free via scan of Cisco AMP.

Correspondence concerning this amendment should be directed to James Connell, Associate Director, Regulatory Affairs, at (614) 272-4709. In my absence, please contact Shane Shupe, Director, Regulatory Affairs, at (681) 781-0996.

Respectfully,

James Connell
Associate Director, Regulatory Affairs
Hikma Pharmaceuticals USA Inc.
Email: dra-columbus@hikma.com