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RESPONSE TO PREA NON-COMPLIANCE LETTER

January 7, 2026

Leah Crisafi, MD, FASA
Director, Division of Anesthesiology, Addiction Medicine, and Pain Medicine
Office of Drug Evaluation II
Food and Drug Administration
Center for Drug Evaluation and Research
5901-B Ammendale Road
Beltsville, MD 20705-1266
USA

Re: NDA 209510
Sequence No.: 0302
Barhemsys (amisulpride) Solution for Injection
Indication: Post-Operative Nausea and Vomiting
Sponsor: Acacia Pharma Ltd, an indirect wholly owned subsidiary of Eagle Pharmaceuticals, Inc. (the "Company")

Dear Dr. Crisafi,

Reference is made to Acacia's NDA for Barhemsys (amisulpride) solution for injection, which was approved on February 26, 2020. Further reference is made to the Agency's Notification of Non-Compliance with PREA letter dated November 24, 2025, and received via email on November 25, 2025, pertaining thereto. A copy of the Agency's communication is provided herein for reference.

We acknowledge the Agency's determination that we have not met the post marketing requirements (PMRs) of the Pediatric Research Equity Act (PREA) for this application due to not submitting NDA 209510 pediatric assessments for the following PMRs:

> **3478-2:** Randomized, double-blind, placebo-controlled, dose-ranging study of Barhemsys (amisulpride) for I.V. injection as prophylaxis for postoperative nausea and vomiting in children aged 0-17 years.
>
> **3478-3:** Randomized, double-blind, active-controlled, dose-ranging study of Barhemsys (amisulpride) for I.V. injection as treatment of children aged 0-17 years with postoperative nausea and vomiting.

Pursuant to 21 U.S.C. 355c(d)(1) and 355c(a)(4)(B), the Company hereby submits a response to the Agency's PREA non-compliance communication dated November 24, 2025.

SPONSOR RESPONSE

Background

We refer the Agency to the DSUR for IND 114207 dated February 7, 2025 (Sequence 0103) and our NDA Annual Report dated April 24, 2025 (Sequence 0291) which provided an update on the

PREA PMRs for this NDA as described in the NDA approval letter dated February 26, 2020. We refer also to our December 20, 2024, meeting request and January 17, 2025, meeting package, pertaining thereto.

As detailed in these materials, Barhemsys was approved on February 26, 2020, with three (3) PREA PMRs, including one (1) juvenile animal toxicity study (PMR 3478-1) (which is completed) and two (2) pediatric clinical studies (3478-2 and 3478-3) (which remain outstanding). Eagle Pharmaceuticals, Inc. (Eagle) acquired Acacia on June 9, 2022.

Following the initial NDA approval, Acacia initiated PMR activities with the intent to fulfill the PMRs in accordance with the approved timelines. When Eagle completed its acquisition of Acacia on June 9, 2022, Eagle inherited the Barhemsys PMRs with the work that was completed as of the acquisition date and milestone dates that were established prior to its acquisition of Acacia. At this time, Acacia had not yet submitted draft protocols to FDA for PMRs 3478-2 and 3478-3, even though they were due in October 2020, almost two years prior.

Eagle quickly addressed these PMRs, and Acacia submitted a protocol (DP10027) in September 2022 for PMR 3478-2 (Sequence 0086 to IND 114207), three months after the Eagle acquisition. Since this initial submission, there were two (2) primary delays. First, developing a protocol and securing agreement from the Competent Authorities, including FDA, required an extensive amount of time. Due to this delay, the first patient was not dosed until (b) (4), and patient recruitment was slower than expected due to the FDA requirement for continuous Holter monitoring for at least 2 hours after study drug administration.

It is also noted with respect to PREA PMR 3478-3, that we advised the Agency that several critical points outlined by the Agency in their Advice/Information Request letter dated November 26, 2024 would be more easily resolved when the data from Study DP10027 are available

Accordingly, we provide the following updates with respect to the outstanding PREA PMRs:

Business and PREA PMR Status

Eagle has executed an (b) (4) with (b) (4) which will transfer the asset, NDA ownership and all regulatory and compliance obligations to (b) (4), including the PREA obligations. During the transition period, Eagle will collaborate with (b) (4) relative to the PREA PMRs to ensure the remaining PREA obligations are addressed.

PREA PMR 3478-2

Eagle has executed this PREA PMR in good faith despite the challenges discussed above. Patient enrollment is complete. Submission of the final clinical study report (CSR) is currently targeted for April of 2026. During the Barhemsys asset transition period, Eagle will coordinate with (b) (4) on the database lock and issuance of the final clinical study report (CSR). Updates/revisions to the prescribing information will be submitted, as appropriate, upon assessment of the final study results. It is acknowledged that this PREA PMR may not be considered fulfilled until results of this study are included in the prescribing information and a labeling or efficacy supplement may be required.

PMR 3478-3

As noted above, we refer the Agency to IND 114207 Amendment dated March 4, 2025 (Sequence 0105), which stated that several critical points outlined by the Agency in their Advice/Information Request letter dated November 26, 2024 would be more easily resolved when the data from Study DP10027 are available. The dosing, PK and safety information from the

prophylaxis study (DP10027) are essential for the optimal, final design of the treatment study DP10028. Further, demonstration of the safety of Barhemsys in pediatric patients in study DP10027, which is now complete, will ensure recruitment of patients for study DP10028 is more feasible.

In consideration of the transition of NDA 212295 and corresponding IND to (b) (4), a revised and final protocol for study DP10028 will be submitted upon assessment and evaluation of the study results of DP10027. (b) (4) will correspond with the Agency accordingly.

We trust the above adequately responds to the Agency's PREA non-compliance communication of November 24, 2025, for PMRs 3478-2 and 3478-3. Furthermore, as requested by the Agency, a cross-reference letter will be submitted to the IND to which our protocol has been submitted (IND 114207, Sequence 00106). If any further information is required or if there are additional questions, please do not hesitate to contact me directly.

This submission has been provided in eCTD format in accordance with the eCTD specifications described in current guidance. An Electronic Submission Specifications form from our publishing vendor (Accenture LLP) is provided as an attachment to this cover letter. A letter of non-repudiation authorizing Accenture to provide electronic signatures on behalf of the Company was submitted to FDA on December 29, 2016.

Sincerely,

Marc Stern (on behalf of Janis Picurro)

Digitally signed by Marc Stern (on behalf of Janis Picurro)
Date: 2026.01.07 14:07:51 -05'00'

Janis A. Picurro
Senior Vice President, Regulatory Affairs
Eagle Pharmaceuticals, Inc.
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NDA 209510

NOTIFICATION OF
NON-COMPLIANCE WITH PREA

Acacia Pharma Ltd
c/o Eagle Pharmaceuticals, Inc.
Attention: Janis A. Picurro
Senior Vice President, Regulatory Affairs
50 Tice Boulevard, Suite 315
Woodcliff Lake, NJ 07677

Dear Janis Picurro,

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Barhemsys (amisulpride) injection, which was approved on February 26, 2020.

The Agency has determined that you have failed to meet the postmarketing requirements (PMRs) of the Pediatric Research Equity Act (PREA) for this application because you have not yet submitted your pediatric assessment for the following:

PMR 3478-2 and PMR 3478-3, which were deferred until 6/30/2024.

Under the provisions of section 505B(d)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) [21 U.S.C. 355c(d)(1)], you must respond in writing within 45 calendar days of the date of this letter. Your response should include the reason(s) for the delayed pediatric assessment and a date by which you expect to submit the assessment. We note that you requested a deferral extension on 4/30/2024; however, we have determined that your request did not qualify for an extension.

In accordance with the FD&C Act, FDA will post this letter and your response to the website at https://www.fda.gov/drugs/development-resources/non-compliance-letters-under-505bd1-federal-food-drug-and-cosmetic-act with redactions for any trade secrets and confidential commercial information 60 calendar days from the date of this letter.

Please identify your response to this letter as a "**RESPONSE TO PREA NON-COMPLIANCE LETTER.**" To facilitate our review, submit this information to your NDA with a cross-reference letter to the investigational new drug application (IND) to which your protocol has been submitted.

If you have any questions, contact Mary Chung, Regulatory Project Manager, at (301)796-0260 or Mary.Chung@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Erica Lyons, M.D.
Associate Director for Therapeutic Review
Division of Gastroenterology
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

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/

ERICA M LYONS
11/24/2025 03:46:53 PM

Electronic Submission Specifications

This submission is compliant with FDA's Guidelines for Industry and current eCTD specifications.

All files were checked and verified to be free of viruses prior to transmission through the electronic submission gateway.

Anti-Virus Program	Microsoft Defender Antivirus
Program Version	4.18.25110.6
Virus Definition Date	01/06/2026
Submission Size	Approx. 4.42 MB