NDA 220544

COMPLETE RESPONSE

Ascelia Pharma AB
c/o Syneos Health
Attention: Anju Mainra
Senior Director
Global Regulatory Affairs Solutions
1030 Sync Street
Morrisville, NC 27560

Dear Anju Mainra:

Please refer to your new drug application (NDA) dated and received September 3, 2025, and your amendments, submitted pursuant to [redacted] for [redacted] (manganese chloride tetrahydrate – powder for oral solution).

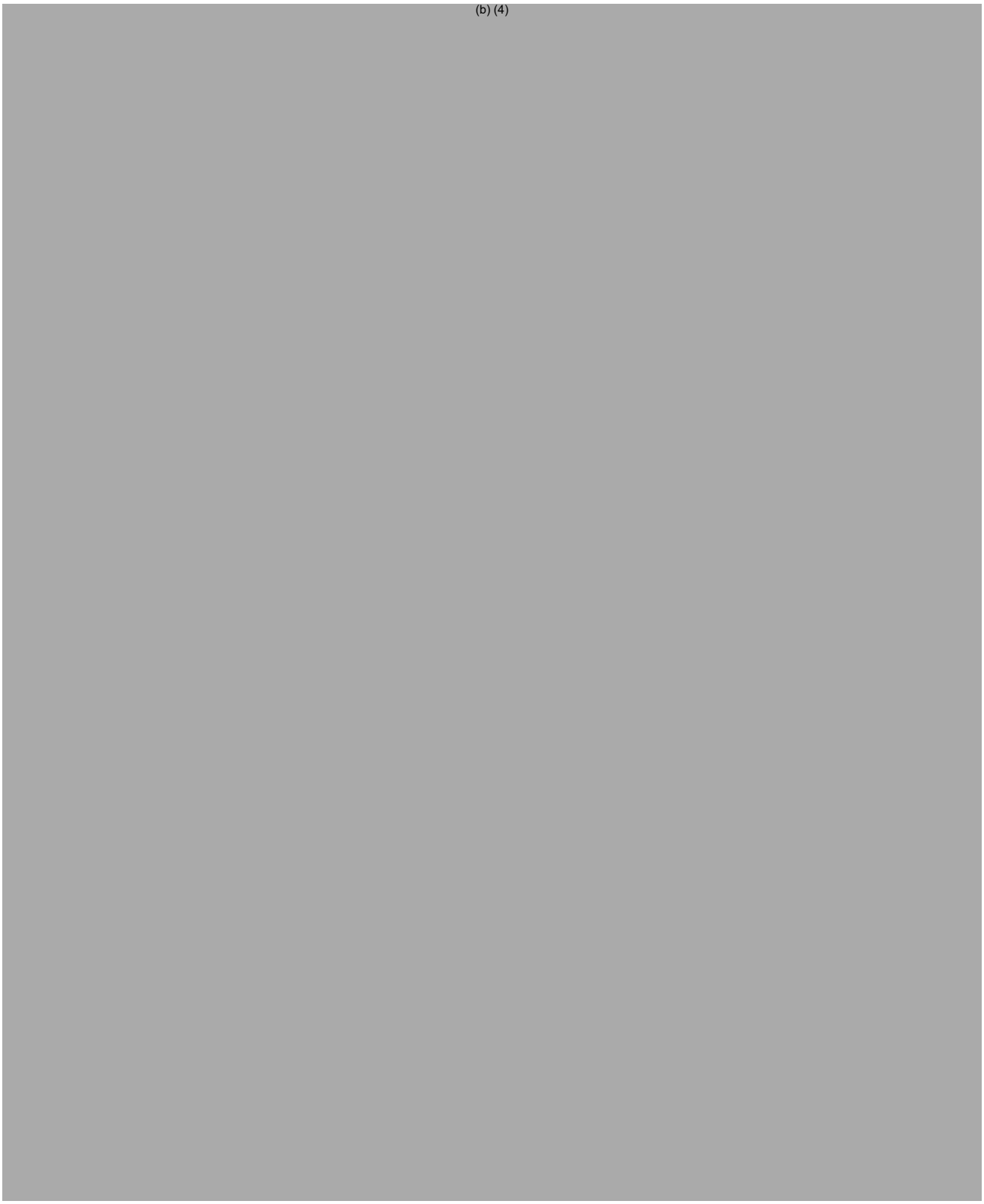
We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

CLINICAL/STATISTICAL

1. ASC-Man-P016, which was submitted as the single adequate and well-controlled study in this NDA, did not meet its pre-specified success criteria since only one of the initial three readers demonstrated superiority of combined pre- and post-[redacted] images to pre-contrast images alone for both lesion contrast and lesion border delineation co-primary endpoints. The post hoc re-evaluation of images from ASC-Man-P016 was not adequately justified and may have introduced bias in the training of the new readers due to knowledge of the images and initial read results. Furthermore, the re-evaluation limited lesion scoring to T1-weighted images and therefore cannot demonstrate that post-[redacted] images provide additional clinical utility beyond standard of care non-T1-weighted images. Thus, the re-evaluation of ASC-Man-P016, which initially did not achieve its pre-specified success criteria, is not considered to be adequate and well-controlled. In the absence of a successful adequate and well-controlled study, substantial evidence of effectiveness has not been demonstrated. We recommend the conduct of a new adequate and well-controlled study with appropriate reader training that includes lesion scoring with the complete set of pre-contrast images.

PRODUCT QUALITY

(b) (4)



(b) (4)

PRESCRIBING INFORMATION

We reserve comment on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the Prescription Drug Labeling Resources[1] and Pregnancy and Lactation Labeling Final Rule[2] websites, including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances.

CARTON AND CONTAINER LABELING

We reserve comment on the proposed labeling until the application is otherwise adequate.

PROPRIETARY NAME

Please refer to our correspondence dated December 1, 2025, which addresses the proposed proprietary name, (b) (4). This name was found conditionally acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to all of the application deficiencies that have been identified in this letter.

SAFETY UPDATE

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(*b*). The safety update should include data from all nonclinical and clinical studies/trials of (b) (4) under consideration regardless of indication, dosage form, or dose level.

(1) Describe in detail any significant changes or findings in the safety profile.

(2) When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:

- Present new safety data from the studies/clinical trials for the proposed indication using the same format as in the original submission.

[1] https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources
[2] https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule

- Present tabulations of the new safety data combined with the original application data.

- Include tables that compare frequencies of adverse events in the original application with the retabulated frequencies described in the bullet above.

- For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.

(3) Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.

(4) Provide case report forms and narrative summaries for each subject who died during a clinical trial or who did not complete a trial because of an adverse event. In addition, provide narrative summaries for serious adverse events.

(5) Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original application data.

(6) Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).

(7) Provide a summary of worldwide experience on the safety of (b) (4). Include an updated estimate for (b) (4) marketed in other countries.

(8) Provide English translations of current approved foreign labeling not previously submitted.

POSTMARKETING REQUIREMENTS UNDER 505(o)(3)

As described in our General Advice letter dated June 11, 2026, we anticipate that, if this application is approved, you may be required to conduct a postmarketing study to identify any unexpected serious risk of exposure to (b) (4) in breastfed infants.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application.

A resubmission must fully address all the deficiencies listed in this letter and should be clearly marked with "**RESUBMISSION**" in large font, bolded type at the beginning of the cover letter of the submission. The cover letter should clearly state that you consider this resubmission a complete response to the deficiencies outlined in this letter. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.

The product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, contact (b) (4) .

Sincerely,

{See appended electronic signature page}

(b) (4)

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/

(b) (4)

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