

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**216686Orig1s000**

**OTHER ACTION LETTERS**



NDA 216686

**COMPLETE RESPONSE**

Spes Pharmaceuticals Inc.  
Attention: Jianwei Yu, PhD  
President, CEO and CSO  
675 US Highway 1, Suite 118  
North Brunswick, NJ 08902

Dear Dr. Yu:

Please refer to your new drug application (NDA) dated December 22, 2021, received December 23, 2021, pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA), for fosaprepitant injection, 150 mg/50 mL (3 mg/mL).

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.

**PRODUCT QUALITY/FACILITY INSPECTIONS**

1. During a recent inspection of the Pharmaceuticals International, Inc. (FEI 3006503102) manufacturing facility for this application, our field investigator conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.
2. During a recent inspection of the Pharmaceuticals International, Inc. (FEI 1000513101) manufacturing facility for this application, our field investigator conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.

**PRESCRIBING INFORMATION**

When you respond to the above deficiencies, submit draft labeling that is responsive to our electronic communications dated August 23, 2022 (Prescribing Information) and August 24, 2022 (Patient Package Insert).

Prior to resubmitting the labeling, use the SRPI checklist to correct any formatting errors to ensure conformance with the format items in regulations and guidances. In addition,

submit updated content of labeling [21 CFR: 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at FDA.gov.<sup>1</sup>

To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Word version. The marked-up copy should include annotations that support any proposed changes.

Your proposed Prescribing Information (PI) must conform to the content and format regulations found at 21 CFR 201.56(a) and (d) and 201.57. As you develop your proposed PI, we encourage you to review the labeling review resources on the Prescription Drug Labeling Resources<sup>2</sup> and Pregnancy and Lactation Labeling Final Rule<sup>3</sup> websites, which include:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- The Final Rule (Pregnancy and Lactation Labeling Rule) on the content and format of information in the PI on pregnancy, lactation, and females and males of reproductive potential
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of important format items from labeling regulations and guidances.
- FDA's established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading.
- Additional resources for the PI, patient labeling, and carton/container labeling.

## **CARTON AND CONTAINER LABELING**

When you respond to the above deficiencies, submit draft carton and container labeling that is responsive to our electronic communication dated August 23, 2022. In addition, revise the container label as shown in Table 1.

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> <https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources>

<sup>3</sup> <https://www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule>

Table 1: Identified Issues and Recommendations for the Container Label

Identified Issue	Rationale for Concern	Recommendation
We note that you are planning to use a hanger strap to administer the product, but it is unclear if the hanger label is transparent.	The hanger attached to the infusion container should not interfere with the ability to read the drug product information on the label. Additionally, the hanger should be transparent and a separate component of the label, as opposed to a portion of the drug label itself. <sup>4</sup>	Ensure that the hanger attached to the infusion container does not interfere with the readability of the drug product information on the label, is transparent in nature and is separate from the label itself.
Container label is missing graduation marks on the side of the label.	Having graduation marks on the infusion container can help health care practitioners identify the amount of drug that remains in the infusion container during administration. <sup>4</sup>	Consider adding graduation marks in milliliters to the infusion container. The graduation marks should be readable when the infusion container is hung upside down for administration.

**PROPRIETARY NAME**

Please refer to correspondence dated, April 20, 2022, which addresses the proposed proprietary name, Focinvez. 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 the application deficiencies.

**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 the drug 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:

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<sup>4</sup> Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors. Food and Drug Administration. 2022. Available from <https://www.fda.gov/regulatoryinformation/search-fda-guidance-documents/safety-considerations-container-labels-and-carton-labeling-design-minimize-medication-errors>

- Present new safety data from the studies/clinical trials for the proposed indication using the same format as in the original submission.
  - 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 re-tabulation of the reasons for premature trial discontinuation by incorporating the dropouts 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 this drug. Include an updated estimate of use for drug marketed in other countries.
  8. Provide English translations of current approved foreign labeling not previously submitted.

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

If you have any questions, call Maureen Dewey, Senior Regulatory Project Manager, at (301) 796-0845.

Sincerely,

*{See appended electronic signature page}*

Joyce Korvick, MD, MPH  
Deputy Director for Safety  
Division of Gastroenterology  
Office of Immunology and Inflammation  
Office of New Drugs  
Center for Drug Evaluation and Research

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**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.**  
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/s/  
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JOYCE A KORVICK  
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