

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**209472Orig1s000**

**OTHER ACTION LETTERS**



NDA 209472

**TENTATIVE APPROVAL**

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

Dear Ms. Picurro:

Please refer to your new drug application (NDA) submitted and received on December 30, 2016, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Pemfexy (pemetrexed injection) 25 mg/mL.

We acknowledge receipt of your amendment dated August 9, 2019, which constituted a complete response to our October 26, 2017, action letter.

This NDA provides for the use of Pemfexy:

- in combination with cisplatin for the initial treatment of patients with locally advanced or metastatic, non-squamous, non-small cell lung cancer (NSCLC);
- as a single agent for the maintenance treatment of patients with locally advanced or metastatic non-squamous NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy;
- as a single agent for the treatment of patients with recurrent, metastatic non-squamous NSCLC after prior chemotherapy; and
- in combination with cisplatin for the initial treatment of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery

We have completed our review of this application, as amended. It is tentatively approved under 21 CFR 314.105 for use as recommended in the agreed-upon enclosed labeling (text for the Prescribing Information, Patient Package Insert, and Carton and Container labeling). This determination is based upon information available to the Agency at this time, [i.e., information in your application and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacture and testing of

the drug product]. This determination is subject to change on the basis of any new information that may come to our attention.

Final approval of your application is subject to expiration of a period of patent protection and/or exclusivity. Therefore, final approval of your application under section 505(c)(3) of the Act [21 U.S.C. 355(c)(3)] may not be granted before the period has expired.

A listed drug(s) upon which your application relies is subject to a period of patent protection and your application contains a certification(s) to one or more patents under section 505(b)(2)(A)(iv) of the FD&C Act stating that the patent(s) is/are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of, this drug product under this application (“paragraph IV certification”).

Section 505(c)(3)(C) of the FD&C Act provides that approval of a new drug application submitted pursuant to section 505(b)(2) of the FD&C Act that includes a paragraph IV certification shall be made effective immediately, unless an action is brought for infringement of one or more of the patents that were the subject of a paragraph IV certification. If such a patent infringement action is brought prior to the expiration of 45 days from the later of the date the notice provided under section 505(b)(3) is received by the patent owner or approved application holder, your application is subject to a 30-month stay of approval, unless other conditions are met. You notified us that you complied with the requirements of section 505(b)(3) of the FD&C Act.

In addition, you have notified the Agency that the patent owner and/or approved application holder has initiated a patent infringement suit against you with respect to patent 7,772,209 in the District Court of Delaware (Civil Action No. 17-cv-1293). Therefore, final approval cannot be granted until:

- (1)
  - a. expiration of the 30-month period provided for in section 505(c)(3)(C) beginning on the later of the date of receipt by any owner of the listed patent or application holder of the notice required under section 505(b)(3), unless the court has extended or reduced the period because of the failure of either party to reasonably cooperate in expediting the action, or
  - b. the date the court decides that the patent(s) is/are invalid or not infringed as described in section 505(c)(3)(C)(i), (ii), (iii,) or (iv) of the FD&C Act, or,
  - c. the listed patent(s) has/have expired, and
- (2) we are assured there is no new information that would affect whether final approval should be granted.

To obtain final approval of this application, submit an amendment two or six months prior to the: (1) expiration of the patent or (2) date you believe that your NDA will be eligible for final approval, as appropriate. In your cover letter, clearly identify your amendment as “**REQUEST FOR FINAL APPROVAL**”. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy

of any relevant court order or judgment settlement, or licensing agreement, as appropriate. In addition to a safety update, the amendment should also identify changes, if any, in the conditions under which your product was tentatively approved, i.e., updated labeling; chemistry, manufacturing, and controls data; and risk evaluation and mitigation strategy (REMS). If there are no changes, clearly state so in your cover letter. Any changes require our review before final approval and the goal date for our review will be set accordingly.

Until we issue a final approval letter, this NDA is not approved.

Please note that this drug product may not be marketed in the United States without final agency approval under section 505 of the FD&C Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 501 of the FD&C Act and 21 U.S.C. 331(d)..

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We note that if this application is ultimately approved, you will need to meet these requirements.

### **METHODS VALIDATION**

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

If you have any questions, call Autumn Zack-Taylor, M.S., Regulatory Health Project Manager, at (240) 402-5913, or in her absence, Meredith Libeg, Senior Regulatory Health Project Manager, at (301) 796-1721.

Sincerely,

*{See appended electronic signature page}*

Jeffery Summers, M.D.  
Deputy Director of Safety  
Division of Oncology Products 2  
Office of Hematology and Oncology Products  
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- Carton and Container Labeling

34 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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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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JEFFERY L SUMMERS  
10/09/2019 05:11:18 PM



NDA 209472

**TENTATIVE APPROVAL**

Eagle Pharmaceuticals, Inc.  
Attention: Adrian Hepner, M.D., Ph.D.  
Chief Medical Officer  
50 Tice Boulevard, Suite 315  
Woodcliff Lake, NJ 07677

Dear Dr. Hepner:

Please refer to your New Drug Application (NDA) submitted and received December 30, 2016, and your amendments, submitted under section 505(b)/pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Pemfexy (pemetrexed injection) 25 mg/mL.

This NDA provides for the use of Pemfexy (pemetrexed injection) 25 mg/mL for the treatment of patients with

- locally advanced or metastatic nonsquamous non-small cell lung cancer in combination with cisplatin;
- locally advanced or metastatic nonsquamous non-small cell lung cancer whose disease has not progressed after four cycles of platinum-based first-line chemotherapy, as maintenance treatment;
- (b) (4) metastatic nonsquamous non-small cell lung cancer after prior chemotherapy as a single agent; and
- malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery in combination with cisplatin.

We have completed our review of this application, as amended. It is tentatively approved under 21 CFR 314.105 for use as recommended in the agreed-upon enclosed labeling (text for the package insert, patient package insert, and carton and immediate container labels). This determination is based upon information available to the Agency at this time, [i.e., information in your application and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacture and testing of the drug product]. This determination is subject to change on the basis of any new information that may come to our attention.

The listed drug upon which your application relies is subject to a period of patent protection and therefore final approval of your application under section 505(c)(3) of the Act [21 U.S.C. 355(c)(3)] may not be made effective until the period has expired.

Your application contains certifications to each of the patents under section 505(b)(2)(A)(iv) of the Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of, this drug product under this application (“Paragraph IV certifications”).

Section 505(c)(3)(C) of the Act provides that approval of a new drug application submitted pursuant to section 505(b)(2) of the Act shall be made effective immediately, unless an action is brought for infringement of one or more of the patents that were the subject of the paragraph IV certifications. This action must be taken prior to the expiration of forty-five days from the date the notice provided under section 505(b)(3) is received by the patent owner/approved application holder. You notified us that you complied with the requirements of section 505(b)(3) of the Act.

In addition, you have notified the Agency that the patent owner and/or approved application holder has initiated a patent infringement suit against you with respect to patent 7,772,209 in the District Court of Delaware (Civil Action No. 17-cv-1293). Therefore, final approval cannot be granted until:

1. a. expiration of the 30-month period provided for in Section 505(c)(3)(C) beginning on the date of receipt of the 45-day notice required under Section 505(b)(3), unless the court has extended or reduced the period because of the failure of either party to reasonably cooperate in expediting the action, or
- b. the date the court decides that the patent is invalid or not infringed as described in section 505(c)(3)(C)(i), (ii), (iii,) or (iv) of the Act, or,
- c. the listed patent has expired, and
2. we are assured there is no new information that would affect whether final approval should be granted.

To obtain final approval of this application, submit an amendment two or six months prior to the: 1.) expiration of the patent or 2.) date you believe that your NDA will be eligible for final approval, as appropriate. In your cover letter, clearly identify your amendment as **“REQUEST FOR FINAL APPROVAL”**. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of any relevant court order or judgment settlement, or licensing agreement, as appropriate. In addition to a safety update, the amendment should also identify changes, if any, in the conditions under which your product was tentatively approved, i.e., updated labeling; chemistry, manufacturing, and controls data; and risk evaluation and mitigation strategy (REMS). Before submitting your amendment, we also recommend you review the updated prescribing information for another approved product as an example [e.g., Alimta (pemetrexed for injection) for intravenous use]. If there are no changes in your amendment, clearly state so in your cover letter. Any changes require our review before final approval and the goal date for our review will be set accordingly.

Until we issue a final approval letter, this NDA is not deemed approved.



Please note that this drug product may not be marketed in the United States without final agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 331(d).

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

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If you have any questions, call Autumn Zack-Taylor, M.S., Regulatory Health Project Manager, at (240) 402-5913.

Sincerely,

*{See appended electronic signature page}*

Joseph Gootenberg, M.D.  
Deputy Division Director  
Division of Oncology Products 2  
Office of Hematology and Oncology Products  
Center for Drug Evaluation and Research

### ENCLOSURE(S):

Content of Labeling  
Carton and Container Labeling

42 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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JOSEPH E GOOTENBERG  
10/26/2017