

BLA 761111

## BLA APPROVAL

Hospira, Inc., a Pfizer Company  
Attention: Neeti Arora, PhD  
Director, Global Regulatory Lead, Global Product Development  
275 North Field Drive  
Dept. 0389, Bldg. H1  
Lake Forest, IL 60045-5046

Dear Dr. Arora:

Please refer to your biologics license application (BLA) dated June 10, 2019, received June 10, 2019 and your amendments, submitted under section 351(k) of the Public Health Service Act for Nyvepria (pegfilgrastim-apgf) injection.

### **LICENSING**

We have approved your BLA for Nyvepria (pegfilgrastim-apgf) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Nyvepria under your existing Department of Health and Human Services U.S. License No. 1974. Nyvepria is indicated for use to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

### **MANUFACTURING LOCATIONS**

Under this license, you are approved to manufacture pegfilgrastim-apgf intermediate at Hospira Adelaide Pty Ltd, a Pfizer company in Thebarton, Adelaide, Australia and pegfilgrastim-apgf drug substance at Hospira Zagreb d.o.o., a Pfizer company in Prigorje Brdovečko Croatia. The final formulated drug product will be manufactured, filled, labeled, and packaged at Hospira Zagreb d.o.o., a Pfizer Company, Zagreb, Croatia. You may label your product with the proprietary name, Nyvepria, and market it in 6 mg/0.6 mL injection in a single-dose prefilled syringe.

### **DATING PERIOD**

The dating period for Nyvepria shall be 36 months from the date of manufacture when stored at  $5\pm 3$  °C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substance shall be <sup>(b) (4)</sup> months from the date of manufacture when stored at <sup>(b) (4)</sup> °C.

We have approved the stability protocols in your license application for the purpose of extending the expiration dating of your DS intermediate (FI), drug substance, and drug product under 21 CFR 601.12.

### **FDA LOT RELEASE**

You are not currently required to submit samples of future lots of Nyvepria to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of Nyvepria, or in the manufacturing facilities, will require the submission of information to your biologics license application for our review and written approval, consistent with 21 CFR 601.12.

### **APPROVAL & LABELING**

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

### **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at FDA.gov.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (Prescribing Information, Patient Package Insert, and Instructions for Use). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.<sup>2</sup>

The SPL will be accessible via publicly available labeling repositories.

### **CARTON AND CONTAINER LABELING**

Submit final printed carton and container labeling that are identical to the carton and container labeling submitted on March 13, 2020 as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related*

---

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

<sup>2</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

*Submissions Using the eCTD Specifications.* For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved BLA 761111**” Approval of this submission by FDA is not required before the labeling is used.

## **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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are deferring submission of your pediatric assessments for patients less than 45 kg until October 2025 for this application.

Your deferred pediatric assessments required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are a postmarketing requirement. The status of this postmarketing requirement must be reported annually according to 21 CFR 601.28 and section 505B(a)(4)(B) of the Federal Food, Drug, and Cosmetic Act. This postmarketing requirement is listed below.

3825-1      Submit pediatric assessments for Nyvepria (pegfilgrastim-apgf) as described in section 505B(a)(2)(A) of the FD&C Act, including development of an “appropriate formulation” (presentation) that can be used to directly and accurately administer NYVEPRIA (pegfilgrastim-apgf) to pediatric patients who weigh less than 45 kg and require doses that are less than 0.6 mL (6 mg), and conducting any necessary human factors studies to evaluate the ability of healthcare providers and/or caregivers to measure the appropriate doses.

Final Report Submission: 10/2025

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.<sup>3</sup> Submit the protocol(s) to your IND 124793, with a cross-reference letter to this BLA. Reports of these required pediatric assessments must be submitted as a BLA or as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission “**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**” in large font, bolded type at the beginning of the cover letter of the submission.

<sup>3</sup> See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019)*.

<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

U.S. Food and Drug Administration

Silver Spring, MD 20993

[www.fda.gov](http://www.fda.gov)

**POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B**

We remind you of your postmarketing commitments:

3825-2 To perform a simulated shipping validation study representing real world shipping conditions, such as temperature, mode of transport, shipping duration, and packaging configuration using PF-06881894 drug product representative of commercial drug product to confirm that product quality is maintained. The simulated shipping validation data will be submitted in accordance with 21 CFR 601.12.

The timetable you submitted on May 29, 2020, states that you will conduct this study according to the following schedule:

Final Report Submission: 08/2020

3825-3 To update the control strategy to include lot release testing for the safety activation force (also referred to as safety device trigger force) of the final finished combination product in order to demonstrate that the product is not more than (NMT) (b)(4)N trigger force.

The timetable you submitted on May 29, 2020, states that you will conduct this study according to the following schedule:

Final Report Submission: 11/2020

**PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.<sup>4</sup>

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.<sup>5</sup> Information and Instructions for completing the form can be found at FDA.gov.<sup>6</sup>

---

<sup>4</sup> For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

<sup>5</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>6</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

## **REPORTING REQUIREMENTS**

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (21 CFR 600.80).

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements for licensed biological products (21 CFR 600.81).

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Compliance Risk Management and Surveillance  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Compliance Risk Management and Surveillance  
10903 New Hampshire Avenue, Bldg. 51, Room 4207  
Silver Spring, MD 20903

## **BsUFA II APPLICANT INTERVIEW**

FDA has contracted with Eastern Research Group, Inc. (ERG) to conduct an independent interim and final assessment of the Program for Enhanced Review Transparency and Communication for Original 351(k) BLAs under BsUFA II ('the Program'). The BsUFA II Commitment Letter states that these assessments will include interviews with applicants following FDA action on applications reviewed in the Program. For this purpose, first-cycle actions include approvals, complete responses, and withdrawals after filing. The purpose of the interview is to better understand applicant experiences with the Program and its ability to improve transparency and communication during FDA review.

ERG will contact you to schedule a BsUFA II applicant interview and provide specifics about the interview process. Your responses during the interview will be confidential

U.S. Food and Drug Administration  
Silver Spring, MD 20993  
[www.fda.gov](http://www.fda.gov)

with respect to the FDA review team. ERG has signed a non-disclosure agreement and will not disclose any identifying information to anyone outside their project team. They will report only anonymized results and findings in the interim and final assessments. Members of the FDA review team will be interviewed by ERG separately. While your participation in the interview is voluntary, your feedback will be helpful to these assessments.

If you have any questions, call Michael Gwathmey, Regulatory Project Manager at (301) 796-8498.

Sincerely,

*{See appended electronic signature page}*

Ann Farrell, MD  
Division Director  
Division of Non-Malignant Hematology  
Office of Cardiology, Hematology,  
Endocrinology, and Nephrology (OCHEN)  
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert or Medication Guide
  - Instructions for Use

-----  
**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/  
-----

ANN T FARRELL  
06/10/2020 02:16:14 PM