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APPLICATION NUMBER:

761080Orig1s000

SUMMARY REVIEW

SUMMARY REVIEW FOR REGULATORY ACTION

Application Number	**BLA 761080**
Application Type	351(k) BLA
Applicant	Hospira, Inc., a Pfizer Company
Date of Receipt	9/21/2017
BSUFA Goal Date	7/21/2018
Division/Office	DHP/OHOP
Division Director	Ann T. Farrell, MD
Proposed Proprietary Name	Nivestym*
Proposed Proper Name	filgrastim-aafi*
Dosage form(s) / Strength(s)	Injection, vial (300 mcg/mL, 480 mcg/1.6mL) Injection, prefilled syringe (300 mcg/0.5mL, 480 mcg/0.8mL)
Applicant's Proposed Indication(s)/Population(s)	• To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever. • For reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML). • To reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation. • For the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis. • To reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.
Recommendation on Regulatory Action	Approval

* For purposes of this review, the proposed product is referred to by either the proprietary name, the proper (nonproprietary) name, or the Sponsor's descriptor PF-06681893. The proposed proprietary name, Nivestym, and the proposed proper name, filgrastim-aafi, are only conditionally accepted until the application is approved.

SUMMARY REVIEW FOR REGULATORY ACTION

On September 21, 2017, Hospira, Inc., a Pfizer Company submitted to the U.S. FDA a biologics license application (BLA 761080) seeking approval of PF-06681893 as a biosimilar to US licensed Neupogen (US-Neupogen). The proposed indications for PF-06681893 are:

- To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
- For reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).
- To reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation.
- For the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.
- To reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia

These are all indications approved for US-Neupogen. Hospira did not seek licensure for the indication to increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome which has unexpired orphan drug exclusivity)[1].

The data and information Hospira provided to support approval of PF-06881893 include:

1) an analytical similarity assessment which compared the properties of PF-06881893 to US-Neupogen to support the demonstration that PF-06881893 is highly similar to US-Neupogen notwithstanding minor differences in clinically active components.
2) Four-week animal toxicology study comparing PF-06881893 with US-Neupogen.
3) Three clinical studies in healthy subjects to support the demonstration that there are no clinically meaningful differences between PF-06881893 and US-Neupogen.

The Product Quality Summary review concluded that PF-06881893is highly similar to US-Neupogen notwithstanding minor differences in clinically active components. The Product Quality Review staff made a recommendation for a post-marketing commitment (b) (4) drug substance endotoxin in-process limits and conduct additional drug substance in-process endotoxin method qualification.

[1] Neupogen's indication for increased survival in patients acutely exposed to myelosuppressive doses of radiation is protected by orphan drug exclusivity expiring on March 30, 2022. See the Orphan Drug Designations and Approvals database at http://www.accessdata fda.gov/scripts/opdlisting/oopd/index.cfm. Accordingly, FDA will not license PF-06881893 for this indication until the orphan drug exclusivity expires.

The Nonclinical review observed that in the toxicology study, PF-06881893 and US-Neupogen produced similar toxicity profiles, pharmacodynamic responses, systemic exposures, and anti-drug antibody responses. The Nonclinical Pharmacology/Toxicology review team identified no residual uncertainties regarding the similarity of PF-06881893 and US-licensed Neupogenand concluded that the application was approvable.

The Clinical Pharmacology review recommended approval of PF-06881893 based on a demonstration of PK and PD similarity and no increase in immunogenicity risk between PF-06881893 and US-Neupogen.

The Clinical review focused primarily on the safety analyses of the data from the three clinical studies submitted to support a demonstration of no clinically meaningful differences between PF-06881893 and US-Neupogen. The clinical reviewer identified no clinically meaningful differences in safety outcomes between PF-06881893 and US-Neupogen.

Inspections

The facilities inspected were considered acceptable. The Applicant claimed a categorical exclusion from the requirement for an environmental assessment, and the claim was accepted under 21 CFR 25.31(c).

The clinical study sites inspection and the BIMO inspection did not uncover any findings which would impact the credibility of the clinical results.

Regulatory recommendation: Approval

I concur with the recommendation of the review teams that PF-06881893 be approved as a biosimilar to US-Neupogen for the following indications:

- To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
- For reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML).
- To reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation.
- For the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.
- To reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

I also concur with the Product Quality Review staff's recommendation for a post-marketing commitment (b) (4) the drug substance endotoxin in-process limits and conduct additional drug substance in-process endotoxin method qualification.

APPEARS THIS WAY ON ORIGINAL

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
07/09/2018