DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 011719/S-126

SUPPLEMENT APPROVAL

Hospira, Inc.
Attention: Erin K. Wierzbicki
Senior Associate
Pfizer Essential Health Global Regulatory Affairs
275 North Field Drive, Bldg H1
Lake Forest, IL 60045

Dear Ms. Wierzbicki:

Please refer to your April 26, 2017, supplemental New Drug Application (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for methotrexate injection, 25 mg/mL (preserved) and methotrexate injection, 25 mg/mL (preservative-free).

We also refer to our letter dated January 8, 2018, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we have determined should be included in the labeling for methotrexate injection. This information pertains to the risk of a serious drug interaction with the use of nitrous oxide potentiating the effect of methotrexate on folate metabolism, resulting in increased toxicity with the use methotrexate injection. Finally, we refer to your February 07, 2018 supplemental New Drug Application (sNDA), containing your proposed safety related labeling changes.

This supplemental new drug application provides for revisions to the labeling for methotrexate injection, 25 mg/mL (preserved) and methotrexate injection, 25 mg/mL (preservative-free), consistent with our January 8, 2018 letter, safety labeling change notification and your March 14, 2018, submission including stomatitis, myelosuppression, and neurotoxicity.

APPROVAL & LABELING

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

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA

automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

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

Because none of these criteria apply to your application, you are exempt from this requirement.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Karen Hennessy, Safety Regulatory Project Manager, at (240) 402-3968.

Sincerely,
{See appended electronic signature page}

Jeffery Summers, M.D.

Deputy Director for Safety
Division of Oncology Products 2
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JEFFERY L SUMMERS
03/15/2018