DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021225/S-032

NDA APPROVAL

Bayer Healthcare Pharmaceuticals, Inc.
Attention: Joseph Zuccarini,
Deputy Director, Global Regulatory Affairs
PO Box 1000
Montville, NJ 07045-1000

Dear Mr. Zuccarini:

Please refer to your Supplemental New Drug Application (sNDA) dated and received February 14, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mirena® (levonorgestrel-releasing intrauterine system) 52 mg.

We also refer to our approval letter dated August 7, 2013, which contained the following error:

1) Attached Product Label was incorrect version.

This replacement approval letter incorporates the correction of the error. The effective approval date will remain August 7, 2013, the date of the original approval letter.

Attached to this replacement letter is the original approval letter with the correct Content of Labeling appended to it. We consider this the approved labeling.

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SUPPLEMENT APPROVAL

Bayer Healthcare Pharmaceuticals, Inc.
Attention: Joseph Zuccarini,
Deputy Director, Global Regulatory Affairs
PO Box 1000
Montville, NJ 07045-1000

Dear Mr. Zuccarini:

Please refer to your Supplemental New Drug Application (sNDA) dated and received February 14, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Mirena® (levonorgestrel-releasing intrauterine system) 52 mg.

This "Changes Being Effected" supplemental new drug application provides for changes to the existing language in the WARNINGS and PRECAUTIONS section, 5.7 subsection Perforation. These changes describe a higher risk of uterine perforation in women who are breastfeeding at the time of insertion.

When the EURAS-IUD study is complete, include in the Final Study Report (FSR) an analysis of the perforation rate by lactating status (yes/no) stratified by

a. time of insertion (immediately after delivery of placenta, > 10 minutes but < 72 hours postpartum, ≥ 72 hours but < 6 weeks postpartum, > 6 weeks postpartum) and
b. by nulliparity status (yes/no).

We have completed our review of this supplemental application. 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, text for patient 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 includes 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.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), 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 http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

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 Charlene Williamson, Senior Regulatory Health Project Manager, at (301) 796-1218.

Sincerely,

{See appended electronic signature page}

Christine P. Nguyen, M.D.
Deputy Director for Safety
Division of Bone, Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

Bayer HealthCare Pharmaceuticals Inc.
Wayne, NJ 07470

Manufactured in Finland

Bayer HealthCare Pharmaceuticals Mirena Hotline - 1-866-647-3646

August 2013

Bayer HealthCare Pharmaceuticals Inc.

6705105

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

/s/

CHRISTINE P NGUYEN
08/07/2013