NDA 021225/S-041

SUPPLEMENT APPROVAL

Bayer HealthCare Pharmaceuticals, Inc
Nancy Velez
Director, Regulatory Affairs Strategy, Women's Health
100 Bayer Boulevard, PO Box 915
Whippany, NJ 07981-0915

Dear Ms. Velez:

Please refer to your supplemental new drug application (sNDA) dated and received September 9, 2020, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Mirena (levonorgestrel-releasing intrauterine system).

This Prior Approval supplemental new drug application provides for changes to the following:

Physician Insert (PI):

Highlights:

- Added Recent Major Changes to indicate a revised Warnings and Precautions subsection

Dosage and Administration Section:

- Recommendation for preinsertion evaluation moved to this section

Warning and Precautions Section

- Updated Risk with Intrauterine Pregnancy subsection language with the risk of virilization

Use in Specific Populations Section

- Updated Pregnancy subsection language with the risk of virilization
- Removed Hepatic Impairment and Renal Impairment subsections

Description

- Updated to specify that colloidal silica is a component of the membrane

Patient Counseling Information

- Updated Risk of Intrauterine Pregnancy language with the risk of virilization

Patient Package Insert (PPI):

- Updated *"Can I use tampons with Mirena?"* subsection to add use of menstrual cups

- Updated "*What if I become pregnant while using Mirena?*", to add discuss possible effects of hormone on unborn baby and encourage discussion with a healthcare provider.

Additional edits to the PI and PPI were made to harmonize with other approved IUS labels.

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 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 FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, 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 *SPL Standard for Content of Labeling Technical Qs and As*.[2]

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 Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), 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 (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

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study(ies) requirement for ages 0 to 11 years and all males because necessary studies are impossible or highly impracticable. This is because the condition does not exist in this age group or gender.

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, Regulatory Project Manager, at (301) 796-1025.

Sincerely,

{See appended electronic signature page}

Audrey Gassman, M.D.
Deputy Director
Division of Urology, Obstetrics and Gynecology
Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert

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/

AUDREY L GASSMAN
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