



NDA 021187/S-035 & S-036

**SUPPLEMENT APPROVAL**

Organon USA Inc., a subsidiary of Merck & Co., Inc.  
Attention: Dajie Li  
Associate Director, Regulatory Liaison, Global Regulatory Affairs  
126 E. Lincoln Avenue  
Rahway, NJ 07065-0900

Dear Mr. Li:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received December 11, 2017 (S-035) and April 17, 2018 (S-036), and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for NuvaRing (etonogestrel and ethinyl estradiol) implants 68 mg.

These Prior Approval supplemental new drug applications provide for (S-035), to add subsection Vaginal Injury (5.18) under Recent Major Changes, Full Prescribing Information and Warning and Precautions Section, and Adverse Reactions Section, Subsection Postmarketing Experience. These changes were also incorporated in the *“What should I tell my healthcare provider before using NuvaRing?”*, and *“What are the possible side effects of using NuvaRing?”*, sections of the Patient Package Insert (PPI).

In addition, for (S-036), changes were made to Hypersensitivity Reactions (5.6) under the Contraindications, Warnings and Precautions, and Adverse Reactions Sections, Subsection Postmarketing Experience to add anaphylaxis and angioedema to the Immune system disorders. These changes were also incorporated in the *“What should I tell my healthcare provider before using NuvaRing?”*, and *“What are the possible side effects of using NuvaRing?”*, and *“Other serious risks,”* sections of the Patient Package Insert (PPI).

**APPROVAL & LABELING**

We have completed our review of these supplemental applications, as amended. They are 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 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 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 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 the claimed indication 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 Charlene Williamson, Regulatory Project Manager, at 301-796-1025.

Sincerely,

*{See appended electronic signature page}*

Audrey Gassman, M.D.  
Deputy Director  
Division of Bone, Reproductive and Urologic Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

ENCLOSURE:  
Content of Labeling

-----  
**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  
12/04/2018