



NDA 021529/S-027

SUPPLEMENT APPROVAL

Organon USA LLC, a subsidiary of Organon & Co.
Attention: Jill Freymuller
Director, Global Product and Regulatory Strategy
4000 Chemical Rd, Suite 500
Plymouth Meeting, PA 19462

Dear Jill Freymuller:

Please refer to your supplemental new drug application (sNDA) dated and received December 16, 2024, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Nexplanon (etonogestrel) implant.

We acknowledge receipt of your major amendment dated August 27, 2025, which extended the goal date by three months.

This Prior Approval supplemental new drug application provides for the extension of the duration of use of Nexplanon (etonogestrel) implant from 3 years to 5 years.

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, and 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.

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

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).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

CARTON AND CONTAINER LABELING

We acknowledge your January 12, 2026, submission containing final printed carton and container labeling.

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.

We are waiving the pediatric studies requirement for all pediatric males and pediatric females of premenarcheal age (e.g., from birth to the age of menarche) because necessary studies are impossible or highly impracticable as the condition of pregnancy does not exist in this population. Premenarchal females are not at risk of becoming pregnant and the use of this product before menarche is not indicated.

We note that you have fulfilled the pediatric study requirement for post-menarchal pediatric patients by extrapolation of adult data.

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database at: <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

Section 505-1 of the Food Drug Cosmetic Act (FDCA) authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS) if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of an approved drug outweigh the risks.

The details of the REMS requirements for Nexplanon were outlined in our REMS Notification letter dated March 28, 2025, to ensure the benefits of Nexplanon outweigh the risk of complications due to adverse events related to improper insertion and removal including migration to the brachial plexus and pulmonary vasculature.

We subsequently determined that certain requirements included in the REMS Notification letter (requiring Nexplanon be dispensed to patients only in certain healthcare settings (ETASU C)) and certification of healthcare settings (ETASU B) are not necessary to ensure that the benefits of Nexplanon outweigh the risk described above. At this time, ETASU C and HCS certification under ETASU B are not necessary to ensure that only certified health care providers who have this training as part of the certification requirement dispense Nexplanon for insertion. Instead, we have determined that compliance with health care provider certification requirements (ETASU B) can be monitored and evaluated through ongoing analyses of claims data. Additionally, implementing these requirements under ETASU B and C could impose additional burden on the healthcare delivery system, which we have determined is not necessary to ensure the benefits of Nexplanon outweigh its risks.

Based on our current understanding of this risk described above, we have determined that the REMS must include only the following elements: elements to assure safe use (pharmacies and practitioners that dispense the drug are specially certified (ETASU B), each patient using the drug is subject to certain monitoring (ETASU E)), an implementation system, and timetable for submission of assessments.

Your proposed REMS, submitted on April 25, 2025, amended and appended to this letter, is approved.

The REMS consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

The approved REMS must be fully implemented within 270 calendar days of the date of this letter. Submit all critical transition issues to the Agency as a REMS correspondence within 1 business day after Organon USA LLC becomes aware of the issue and submit all moderate transition issues to the Agency as a REMS correspondence no later than 7 calendar days after Organon USA LLC becomes aware of the issue.

The REMS assessment plan must include, but is not limited to, the following:

For each metric, provide the two previous, current, and cumulative reporting periods (if applicable) unless otherwise noted.

REMS Implementation and Operations

1. REMS Implementation (for the first and second REMS Assessment Reports only)
 - a. Date(s) of Nexplanon REMS launch including:
 - i. The date when the certification process for HCPs who dispense Nexplanon for insertion, and Pharmacies became active
 - ii. The date when wholesalers-distributors were authorized by the REMS to distribute drug
 - iii. The date when REMS Transition Period was complete
 - b. Date when the REMS Coordinating Center became operational
 - c. Date when the **REMS Website** became live and fully operational
 - d. Total number and percentage of previously trained HCPs who transitioned to the REMS and became certified, stratified by method of REMS certification including:
 - i. Certifications for previously trained and active HCPs who are transitioned to the REMS
 - ii. Certification for previously trained inactive HCPs
 - e. Total number and percentage of pharmacies that previously dispensed Nexplanon and now transitioned to the REMS and became certified
 - f. Total number and percentage of wholesalers-distributors that previously distributed Nexplanon and now transitioned to the REMS and became authorized
 - g. Provide an assessment and summary of the reasons (when available) for why any previously trained HCPs did not transition to the REMS. Indicate if burden or patient access issues were identified, and any actions taken to address these issues
2. REMS Certification Statistics
 - a. HCPs who dispense Nexplanon for insertion
 - i. Total number of certified HCPs at the end of the reporting period, stratified by professional designation (i.e., Doctor of Medicine (MD), Doctor of Osteopathic Medicine (DO), Nurse Practitioner (NP), Physician Assistant (PA), Certified Nurse-Midwife (CNM), Other [specify], etc.) and by medical specialty (i.e., Obstetrics/Gynecology, General Practitioner, Internal Medicine, Other [specify], etc.)

- ii. Total number of newly certified HCPs at the end of the reporting period, stratified by professional designation (i.e., Doctor of Medicine (MD), Doctor of Osteopathic Medicine (DO), Nurse Practitioner (NP), Physician Assistant (PA), Certified Nurse-Midwife (CNM), Other [specify], etc.) and by medical specialty (i.e., Obstetrics/Gynecology, General Practitioner, Internal Medicine, Other [specify], etc.)
- iii. Total number of HCPs who dispensed Nexplanon for insertion at least once during the reporting period, stratified by professional designation (i.e., MD, DO, NP, PA, CNM, Other [specify]) and by medical specialty (i.e., Obstetrics/Gynecology, General Practitioner, Internal Medicine, Other [specify], etc.)
- iv. Number of HCPs who dispense Nexplanon for insertion who recertified (i.e., maintained certification) after three years of inactivity.
- v. The number of HCPs who were inactivated, stratified by reason for inactivation (i.e., due to non-response, attesting no, etc.)

b. Healthcare Provider Knowledge Assessment

- i. Summarize the number of HCPs who completed the **Healthcare Provider Knowledge Assessment**. Include method of completion, and the average, minimum, and maximum number of attempts needed to complete
- c. Pharmacies that dispense Nexplanon
- i. Total number of certified Pharmacies as of the end of the reporting period, regardless of whether they dispensed Nexplanon
 - ii. Total number of newly certified Pharmacies as of the end of the reporting period
 - iii. Total number of active (i.e., dispensed Nexplanon at least once during the reporting period) Pharmacies as of the end of the reporting period, regardless of when they were certified
- d. Authorized Wholesalers-Distributors
- i. Total number of authorized wholesalers-distributors as of the end of the reporting period, regardless of whether they distributed Nexplanon

- ii. Total number of newly authorized wholesalers-distributors as of the end of the reporting period
- iii. Total number of active (i.e., have shipped Nexplanon at least once during the reporting period) wholesalers-distributors at the end of the reporting period

3. REMS Operation and Performance Data

a. REMS Coordinating Center

- i. Number and percentage of contacts by type (e.g., HCPs, Pharmacies, patients, wholesalers-distributors, field personnel, other [specify]), stratified by inbound and outbound contacts
 - ii. Number of contacts requesting a referral to the Centers of Experience (COE), including any additional details such as reason for the referral and follow-up/outcome (if available)
 - iii. Summary of reasons for inbound and outbound contacts (e.g., certification question, certified pharmacy/HCP list, notification for recertification/upcoming expiration), stratified by participant type (e.g., HCP, pharmacy, wholesaler-distributor, field personnel); limit to the top five reasons for contact by participant group
- b. Assessment of issues identified or reported to the REMS related to healthcare delivery system burden, or patient access issues. Provide the data source, the results of a root cause analysis, and actions taken to mitigate future occurrences

4. Utilization

- a. Number of Nexplanon units distributed during the reporting period, stratified by recipient (i.e., to HCP and pharmacy)
- b. Number of Nexplanon shipments from wholesalers-distributors stratified by shipment recipient (i.e., to HCP and pharmacy)
- c. Number of Nexplanon units dispensed by pharmacies to HCPs (where available)

- d. Number of units of Nexplanon dispensed by HCPs for insertion during the reporting period. Include a description of the data source(s) used to obtain the dispensing data, including any known limitations of the utilization data source(s) and any methods used to address these limitations
- e. Provide a comparison of Nexplanon utilization before and after REMS implementation. For comparison, evaluate utilization trends for the last 3 years before the REMS to utilization trends following REMS approval. Include the following in the comparison:
 - i. Number of Nexplanon units distributed, stratified by recipient (i.e., to HCP and pharmacy)
 - ii. Number of Nexplanon shipments from wholesalers-distributors stratified by shipment recipient (i.e., to HCP and pharmacy)
 - iii. Number of Nexplanon units dispensed by pharmacies to HCPs (where available)
 - iv. Number of units of Nexplanon dispensed by HCPs for insertion
 - v. Include a description of the data sources for metrics 4.e.i.-iv.

5. REMS Compliance

- a. Audits: Summary of audit activities, including but not limited to the following:
 - i. Copy of audit plan for Pharmacies that dispense Nexplanon and wholesalers-distributors that distribute Nexplanon
 - ii. Number of audits expected per the REMS Document and number of audits performed
 - 1. Reasons for any discrepancies between number of audits expected versus performed and any remedial actions taken
 - iii. Number and type (e.g., critical, major, or minor findings) of deficiencies noted

1. Status of corrective and preventive action (CAPA) proposed to address deficiencies, including completion dates
 2. For any that did not complete the CAPA within the timeframe specified in the audit plan, describe actions taken
 - iv. Confirmation of documentation of completion of training for relevant staff
 - v. Verification of the existence of documented processes and procedures for complying with the REMS
 - vi. A review of previous audit findings and an assessment of whether any trends are observed
- b. Non-compliance: provide a summary of the non-compliance identified, including but not limited to the following:
- i. A copy of the Non-Compliance Plan, which addresses the criteria for non-compliance for each participant, actions taken to address non-compliance for each event, and under what circumstances a participant would be suspended or de-certified from the REMS
 - ii. Number and percentage of certified HCPs who were identified through REMS operations as non-compliant with the REMS requirements including but not limited to the following. For each event, include the source of the report, corrective actions taken to prevent future occurrences, and the outcome of such action:
 1. Number of certified HCPs that had certification suspended or revoked, including the reasons for the action
 2. Total number of HCPs who dispensed Nexplanon for insertion without being certified
 - a. Number of HCPs who dispensed Nexplanon for insertion without having recertified (i.e., maintained certification) after three years of inactivity
 - b. Number of HCPs who dispensed Nexplanon for insertion without ever having certified or completed the clinical training program

- iii. Number and percentage of certified Pharmacies who were identified through REMS operations as non-compliant with the REMS requirements including but not limited to the following. For each event, include the source of the report, corrective actions taken to prevent future occurrences, and the outcome of such actions:
 1. Number of certified Pharmacies that had certification suspended or revoked; include the reasons for the action
 2. Number of units that were dispensed to noncertified HCPs
 3. The number and percentage of Pharmacies that were non-compliant with the requirement to dispense Nexplanon only to certified HCPs. Stratify the results by number of events per non-compliant Pharmacy.
 4. Number of occurrences where Nexplanon was loaned or transferred to a noncertified Pharmacy, and disposition of the drug
- iv. Number of noncertified Pharmacies that dispensed Nexplanon
 1. Summarize the total number of dispenses while noncertified, and the total number of shipments received while noncertified
- v. Number and percentage of authorized wholesalers-distributors that were non-compliant with the REMS requirements including the following. For each event, include the source of the report, corrective actions taken to prevent future occurrences, and the outcome of such action:
 1. Number of shipments (and units) sent to noncertified Pharmacies or noncertified HCPs, and disposition of the drug
- vi. For all non-compliance events, include: the number of instances of non-compliance accompanied by a description of each instance and the reason for the occurrence (if provided). For each instance of non-compliance, report the following information:

1. The unique identifier(s) (ID(s)) of the participant(s) associated with the non-compliance event or deviation to enable tracking over time
 2. Severity categorization (e.g., critical, major, minor)
 3. The source of the non-compliance data for each noncompliant event
 4. The results of the root cause analysis
 5. What corrective and preventive actions were taken in response and if any follow-up was conducted
6. Healthcare Provider Training Compliance (beginning with the 18-month REMS Assessment Report and annually thereafter)
- a. Claims-based analysis of Nexplanon insertion and removal: Using claims data from US claims-based data providers, assess the number, type, and training status of HCPs who perform procedures with Nexplanon including:
 - i. The number of HCPs who perform procedures with Nexplanon by certification status
 - ii. The proportion of HCPs who perform procedures with Nexplanon, by certification status
 - iii. The proportion of HCPs who perform insertion procedures with Nexplanon, by certification status
 - iv. The proportion of HCPs who perform removal procedures with Nexplanon, by certification status
 1. Among HCPs who are non-certified who perform removal procedures with Nexplanon, the proportion that are done “in emergency situations or because of a complicated removal requiring involvement of a surgical specialist”
 - v. For any identified HCP certification non-compliance, conduct a secondary analysis (e.g., a root cause analysis) to inform on the reasons why HCPs who performed procedures were not certified

- vi. For the calculated proportions, indicate all data sources, processing steps, and validation methods applied to the data feeds into the calculation. Provide an assessment of data quality, including completeness rates, accuracy validation, and any known limitations or reliability concerns
- vii. Provide the claims-based analysis protocol/methodology as an appendix

Health Outcomes and/or Surrogates of Health Outcomes

- 7. Insertion and Removal Related Events (IRREs): Provide an analysis of the incidence of IRREs. Analyze factors associated with IRREs, including the association between training (certification) status of the HCP and IRREs. The analyses should include but not be limited to the following:
 - a. Claims-based analyses of IRREs (beginning with the 18-month REMS Assessment Report and annually thereafter)
 - i. The IRRE component endpoint events analyzed and their respective ICD codes from the claims-based analysis
 - ii. A stratified analyses assessing IRREs and their association with certification status
 - 1. A summary that includes all data sources, processing steps, and validation methods applied to the data. Provide an assessment of data quality, including completeness rates, accuracy validation, and any known limitations or reliability concerns
 - b. Analyze US adverse event reports of IRREs. Sources of adverse reports must include **Insertion and Removal-Related Events Documentation Forms** and spontaneous adverse event reports. In your analysis, include the following:
 - i. Include the search strategy used for each data source and the case definition used. Include search dates and specific Medical Dictionary for Regulatory Activities (MedDRA) terms used
 - ii. After de-duplication, provide a tabular summary of the cases including the following:

1. Number of IRRE reports from all sources
 2. Number of IRRE reports from each source
 3. Number of IRRE reports, stratified by Insertion Related Events, Post Insertion Related Events, Removal Related Events
 4. Seriousness (e.g., number of cases categorized as fatal, life-threatening, requiring initial or prolonged hospitalization, disability or permanent damage, etc.)
 5. For Insertion Related Events, number of deep insertions, expulsions, failed/non-insertion, intravascular insertion, partial insertion, and non-palpable insertions
 6. For Post Insertion Related Events, number of migrations, stratified by location
 7. For Removal Related Events, number of events related to difficult removal due to deep implant, nerve injury, fibrosis/scar tissue, intravascular implant, other
 8. Outcome of Event (e.g., recovered/resolved, recovering/resolving, not recovered/not resolved/ongoing, recovered/resolved with sequelae, fatal, unknown)
 9. Assessment of relatedness of Nexplanon to event
 10. Assessment of potential contributing factors to event (e.g., training status)
- iii. For serious confirmed US cases of IRREs involving vascular migrations, device embolization, or nerve injuries only, provide a brief narrative summary. Describe whether there is any association to certification status. Include the case identifier (e.g., manufacturer control number) for each narrative.
 - iv. Include a reference list of case identifiers (e.g., manufacturer control numbers) for all cases included in the analysis above

- c. Provide new or updated safety findings, if any, to inform the incidence, severity, and frequency of IRREs, and an assessment of the effectiveness of the REMS strategy in mitigating the risk

Overall Assessment of REMS Effectiveness

8. The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether 1 or more such goals or such elements should be modified.

If the information provided in an assessment is insufficient to allow FDA to determine whether the REMS is meeting its goals or whether the REMS must be modified, FDA may require the submission of a new assessment plan that contains the metrics and/or methods necessary to make such a determination. Therefore, FDA strongly recommends obtaining FDA feedback on the details of your proposed assessment plan to ensure its success. To that end, we recommend that methodological approaches, study protocols, other analysis plans and assessment approaches used to assess a REMS program be submitted for FDA review as follows:

- i. Submit your proposed audit plan and noncompliance plan for FDA review within 60 days of this letter.
- ii. Submit your proposed claims-based study protocol for FDA review within 60 days of this letter.

Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

NDA 021529 REMS ASSESSMENT METHODOLOGY

(insert concise description of content in bold capital letters, e.g.,

ASSESSMENT METHODOLOGY, PROTOCOL, SURVEY METHODOLOGIES, AUDIT PLAN, DRUG USE STUDY)

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use, as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

- a) An evaluation of how the benefit-risk profile will or will not change with the new indication;
- b) A determination of the implications of a change in the benefit-risk profile for the current REMS;
- c) *If the new, proposed indication for use introduces unexpected risks:* A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.
- d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* A statement about whether the REMS was meeting its goals at the time of that last assessment and if any modifications of the REMS have been proposed since that assessment.
- e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.
- f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including:* Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing a REMS modification, provide a rationale for why the REMS does not need to be modified.*

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted.

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 021529 REMS ASSESSMENT

or

**NEW SUPPLEMENT FOR NDA 021529/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION**

or

**NEW SUPPLEMENT FOR NDA 021529/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION**

or

**NEW SUPPLEMENT FOR NDA 021529/ S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING
CHANGES SUBMITTED IN SUPPLEMENT XXX**

or

**NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 021529/ S-000
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)**

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISION FOR NDA 021529

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, or website screenshots are only in PDF format, they may be submitted as such, but Word format is preferred.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

As soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in Structured Product Labeling (SPL) format using the FDA automated drug registration and listing system (eLIST). Content of the REMS document must be identical to the approved REMS document. The SPL will be publicly available.

Information on submitting REMS in SPL format may be found in the guidance for industry *Providing Regulatory Submission in Electronic Format – Content of the Risk Evaluation and Mitigation Strategies Document Using Structured Product Labeling*.

For additional information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.³

You must submit final promotional materials and Prescribing Information, 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 FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵

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-related information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety-related information that appears in the revised labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4).

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR

³ For the most recent version of a guidance, check the FDA guidance web page at:

<https://www.fda.gov/media/128163/download>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

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

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.⁶

If you have any questions, call or email Jeannie Roule, Chief, Project Management Staff (Jeannie.roule@fda.hhs.gov, 301-796-3993).

Sincerely,

{See appended electronic signature page}

Audrey Gassman, MD
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
- Carton and Container Labeling
- REMS

⁶ <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>

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
01/16/2026 08:17:43 AM