



NDA 221033

NDA APPROVAL

Rosemont Pharmaceuticals Holdings, Inc.
Attention: Korie Osborn
Vice President, Regulatory Affairs
6035 Ponders Court
Suite G
Greenville, SC 29615

Dear Korie Osborn:

Please refer to your new drug application (NDA) received December 18, 2025, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Yulzety (rivaroxaban) oral suspension.

This NDA provides for the use of Yulzety (rivaroxaban) oral suspension for the following indications:

- to reduce risk of stroke and systemic embolism in nonvalvular atrial fibrillation
- for treatment of deep vein thrombosis (DVT)
- for treatment of pulmonary embolism (PE)
- for reduction in the risk of recurrence of DVT or PE
- for the prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery
- for prophylaxis of venous thromboembolism (VTE) in acutely ill medical patients
- for treatment of VTE and reduction in the risk of recurrent VTE in pediatric patients weighing at least 12 kg
- for thromboprophylaxis in pediatric patients, weighing at least 12 kg, with congenital heart disease after the Fontan procedure

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, Instructions for Use, and Medication Guide) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.²

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to guidance for industry *SPL Standard for Content of Labeling Technical Qs & As*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved NDA 221033.**” Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the stability data submitted to date, an expiry dating period of twenty-four (24) months from the date of manufacture is granted for Yulzety (rivaroxaban) oral suspension, 2 mg/mL and 4 mg/mL, when stored at 20°C to 25°C (68°F to 77°F) with excursions permitted from 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

The expiration date for the packaged product, Yulzety plus oral syringe, 5 mL or 10 mL, shall be dependent on the shortest expiration date of any component.

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 deferring submission of your pediatric study for patients weighing less than 12 kg for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

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>.

Your deferred pediatric study required by section 505B(a) of the FD&C Act is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the FD&C Act. This required study is listed below.

5085-1 Develop an "appropriate formulation" (presentation) of rivaroxaban that can be used to directly and accurately administer rivaroxaban to pediatric patients < 12kg. Conduct any necessary human factors studies to evaluate the ability of healthcare providers and caregivers to measure the appropriate doses.

Final Report Submission: January 2029

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial. See guidance for industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act*.

Submit the protocol to your IND 162216, with a cross-reference letter to this NDA. Reports of this required pediatric postmarketing study must be submitted as an NDA or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from this study. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

5085-2 Perform leachable studies on the first three commercial batches for each of the two strengths of Yulzety (rivaroxaban), 2 mg/mL and 4 mg/mL, placed on stability at long-term storage conditions ($25^{\circ}\text{C} \pm 2^{\circ}\text{C}/60\% \text{ RH} \pm 5\% \text{ RH}$, per ICH Q1A) with samples stored in the inverted position and tested at early (0-3 month), middle (6-9 month), late (12-18 month), and end (24-month) timepoints throughout the shelf-life. The requested studies shall include evaluation for both targeted leachables and leachables from non-targeted screening. The targeted leachables evaluation should be based on the compounds detected above the Analytical Evaluation Threshold (AET) in extractable studies for each component of container closure system which has direct contact with the oral suspension during shelf-life.

Based on results obtained from the leachables studies described above, update the AET and recalculate leachable exposure estimates for comparison against the Safety Concern Threshold (SCT) values, accordingly. If any individual leachable compound exceeds the SCT of 1.5 mcg/day, a toxicological risk assessment should be performed based on the maximum level of each leachable detected in long-term stability samples. Copies of all referenced studies upon which a safety assessment is based must be included in the submission.

The timetable you submitted on October 9, 2026, states that you will conduct this study according to the following schedule:

Draft Protocol Submission: January 2027
Final Protocol Submission: March 2027
Interim Report Submission: October 15, 2028
Final Report Submission: October 15, 2029

A final submitted protocol is one that the FDA has reviewed and commented upon, and you have revised as needed to meet the goal of the study or clinical trial.

Submit clinical protocols to your IND 162216 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients/subjects entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **“Postmarketing Commitment Protocol,” “Postmarketing Commitment Final Report,” or “Postmarketing Commitment Correspondence.”**

PROMOTIONAL MATERIALS

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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.³ Information and Instructions for completing the form can be found at FDA.gov.⁴

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.⁵

REQUESTED ENHANCED PHARMACOVIGILANCE (EPV)

We request that for Yulzety you submit all U.S. cases associated with a wrong dose error as though they were 15-day “Alert reports” (which are described under 21 CFR 314.80(c)(1)) through the 3rd year following initial U.S. approval.

We request that you provide a narrative summary including analysis of wrong dose errors as part of your required periodic safety reports (e.g., the periodic adverse drug experience report [PADER] required under 21 CFR 314.80(c)(2)), quarterly during the first 3 years post- approval.

Your analysis should include interval and cumulative data relative to the date of approval of Yulzety. Your analysis should provide the methods (including data sources and search terms) used to identify the cases, assessment of the cases, cumulative line listing of the cases, and the following information:

- The number of cases associated with a suspected or confirmed wrong dose

³ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

⁵ <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>

error, including overdose and underdose, and cases describing the potential for a wrong dose error (e.g., close calls/near misses and circumstances capable of leading to a wrong dose error).

- Patient age, weight, prescribed dose (specified in mg and/or mL), and administered dose.
- Stage of the medication use process where the error originated (e.g., prescribing, dispensing, or administration).
- Contributing factors and causes for the error, e.g., prescribing by volume (mL) instead of mg, unclear Instructions for Use or dosing information, difficulty measuring the prescribed dose, use of the incorrect syringe or confusion with the syringe markings, negative transfer from prior use of other 1 mg/mL rivaroxaban oral liquid products, wrong product dispensed, mix-ups between the 2 mg/mL and 4 mg/mL concentrations, or weights recorded as pounds instead of kilograms.
- Reporter recommendations or actions taken to prevent the error from occurring/recurring.
- Adverse events and outcomes attributed to the error.

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standards for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website⁶.

⁶ <https://www.uspnf.com/>

If you have any questions, please contact Rolanda Bailey, Regulatory Project Manager, at (240) 402-5631 or email at Rolanda.Bailey@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Carrie Diamond, MD
Acting Deputy Division Director
Division of Nonmalignant Hematology
Office of Cardiology, Hematology,
Endocrinology, and Nephrology
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Medication Guide
 - Instructions for Use
- Carton and Container 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/

CARRIE E DIAMOND
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