CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215859Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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Date of This Review:	October 25, 2021
Application Type and Number:	NDA 215859
Product Name and Strength:	Xarelto (rivaroxaban) for oral suspension, 155 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Janssen Pharmaceuticals, Inc. (Janssen)
PNR ID #:	2021-1044724117
DMEPA 2 Safety Evaluator:	Mariette Aidoo, PharmD, MPH
DMEPA 2 Team Leader:	Hina Mehta, PharmD
DMEPA 2 Associate Director for Nomenclature and Labeling:	Chi-Ming (Alice) Tu, PharmD, BCPS

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Xarelto, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A, respectively. Janssen did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Xarelto (rivaroxaban) tablets, was approved on July 1, 2011 under NDA 022406 as an antifactory Xa inhibitor indicated for the treatment of deep vein thrombosis and pulmonary embolism, and the risk reduction of stroke and systemic embolism in nonvalvular atrial fibrillation. Xarelto is currently marketed as 2.5 mg, 10 mg, 15 mg, and 20 mg tablets.

Janssen now proposes NDA 215859 rivaroxaban for oral suspension, 155 mg, supplied in a bottle for the proposed indication of VTE and reduction in the risk of recurrent VTE in pediatric patients from birth to less than 18 years and for thromboprophylaxis in pediatric patients 2 years and older with congenital heart disease after the Fontan procedure.

Thus, Janssen submitted the name, Xarelto, for the newly proposed dosage form for review under NDA 215859 on August 12, 2021.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on August 12, 2021 for Xarelto (rivaroxaban) for oral suspension and the Prescribing Information for Xarelto (rivaroxaban) tablets.

Table 1. Relevant Product Information for Velphoro (sucroferric oxyhydroxide)

Product	**Xarelto [Proposed] (NDA 215859)**	**Xarelto [a] (NDA 022406)**
Initial Approval Date	Under review	July 1, 2011
Intended Pronunciation	Zah-REL-toe	
Active Ingredient	rivaroxaban	
Indication	• for treatment of venous thromboembolism (VTE) and reduction in the risk of recurrent VTE in pediatric patients from birth to less than 18 years.	• To reduce risk of stroke and systemic embolism in nonvalvular atrial fibrillation • For treatment of deep vein thrombosis (DVT)

[a] Xarelto (rivaroxaban) [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2021 AUG 31. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/022406s000lbl.pdf

	for thromboprophylaxis in pediatric patients 2 years and older with congenital heart disease after the Fontan procedure.	• 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 • To reduce the risk of major cardiovascular events in patients with chronic coronary artery disease (CAD) or peripheral artery disease (PAD)
Route of Administration	Oral	
Dosage Form	For oral suspension	Tablets
Strength	Each bottle contains 155 mg of rivaroxaban (1 mg/mL once reconstituted	2.5 mg, 10 mg, 15 mg, 20 mg
Dose and Frequency	Pediatric Patients – 1 mg Xarelto = 1 mL suspension; weight based dosing) <u>Treatment of Venous thromboembolism and reduction in risk of recurrent venous thromboembolism in pediatric patients:</u> • Oral Suspension Only: 2.6 kg to < 12 kg: 2.4 mg up to 9 mg Total Daily Dose (over 3 divided doses) 12 kg to < 30 kg: 10 mg Total Daily Dose (over 2 divided doses) • Oral Suspension or Tablets: 30 kg to < 50 kg: 15 mg once daily ≥ 50 kg: 20 mg once daily.	• <u>Nonvalvular Atrial Fibrillation</u>: 15 or 20 mg, once daily with food. • <u>Treatment of DVT and/or PE</u>: 15 mg orally twice daily with food for the first 21 days followed by 20 mg orally once daily with food for the remaining treatment. • <u>Reduction in the Risk of Recurrence of DVT and/or PE in patients at continued risk for DVT and/or PE</u>: 10 mg once daily with or without food, after at least 6 months of standard anticoagulant treatment. • <u>Prophylaxis of DVT Following Hip or Knee Replacement Surgery</u>: 10 mg orally once daily with or without food. • <u>Prophylaxis of VTE in Acutely Ill Medical Patients at Risk for Thromboembolic Complications Not at High Risk of Bleeding:</u> 10 mg once daily, with or without food, in hospital

	Thromboprophylaxis in Pediatric patients with congenital heart disease after fontan procedure: • Oral Suspension Only: 7 kg to < 30 kg: 2.2 mg up to 5 mg TDD (over 2 divided doses) 30 kg to < 50 kg: 7.5 mg once daily • Oral Suspension or Tablets: ≥ 50 kg: 10 mg once daily. **TDD = Total Daily Dose**	and after hospital discharge for a total recommended duration of 31 to 39 days. • CAD or PAD: 2.5 mg orally twice daily with or without food, in combination with aspirin (75-100 mg) once daily.
Instructions for Use	Tap the bottle until all granules flow freely. Add 150 mL of water for reconstitution. Shake for 60 seconds. Check that all granules are wetted and the suspension is uniform. Push the adaptor into bottleneck and recap bottle. (b) (4) The suspension must be used within 60 days. (b) (4) . ** Dispense the bottle upright with the syringes provided in the original carton.* (b) (4)	Administer with meals or without meals.
How Supplied	•White to off-white granules in an amber glass bottle containing 155 mg rivaroxaban packaged with two oral dosing syringes. Administer via a co-packaged 5 mL ELM oral dosing syringe Certa Dose label.	• 2.5 mg tablets available in: Bottle containing 60 tablets Bottle containing 180 tablets Blister package containing 100 tablets (10 blister cards containing 10 tablets each) • 10 mg and 15 mg tablets available in: Bottle containing 30 tablets Bottle containing 90 tablets Blister package containing 100 tablets (10 blister cards containing 10 tablets each) • 20 mg tablets available in: Bottle containing 30 tablets

		Bottle containing 90 tablets Bulk bottle containing 1000 tablets Blister package containing 100 tablets (10 blister cards containing 10 tablets each) • 30-day starter blister pack containing 51 tablets: 42 tablets of 15 mg and 9 tablets of 20 mg
Storage	Storage of tablets, granules and reconstituted suspension: Store at room temperature between 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].	

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name, Xarelto.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Xarelto would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) and the Division of Cardiology and Nephrology (DCN) concurred with the findings of OPDP's assessment for Xarelto.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Xarelto.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name[b].

2.2.2 Components of the Proposed Proprietary Name

Janssen did not provide a derivation or intended meaning for the proposed proprietary name, Xarelto, in their submission. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

[b] USAN stem search conducted on September 2, 2021.

2.2.3 Comments from Other Review Disciplines at Initial Review

On August 24, 2021, the Division of Cardiology and Nephrology (DCN) did not forward any comments or concerns relating to Xarelto at the initial phase of the review.

2.2.4 Evaluation of a Single Proprietary Name for Multiple Dosage Forms

We note that the newly proposed for oral suspension dosage formulation shares the same active ingredient as the currently approved Xarelto tablets. It is a common and accepted practice to have a product line with multiple dosage forms managed under one proprietary name (e.g. Sevelamer and Pradaxa). Based on our understanding from the prescribing information at the time of this review, the proposed for oral suspension dosage formulation is also equivalent on a mg-per-mg basis with the currently approved Xarelto tablets. Furthermore, we note that through our routine monitoring we have not identified any medication errors involving name confusion with the proprietary name Xarelto. Therefore, given the precedence for using this naming convention, and the absence of any medication errors involving the proprietary name, we find the Sponsor's proposal to market the proposed product with the proprietary name Xarelto acceptable. The difference in the product characteristics between the two dosage formulations for Xarelto may be managed through labels and labeling.

2.2.5 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA 2 communicated our findings to the Division of Cardiology and Nephrology (DCN). At that time we also requested additional information or concerns that could inform our review. On October 21, 2021, the Division of Cardiology and Nephrology (DCN) stated no additional concerns with the proposed proprietary name, Xarelto.

3 CONCLUSION

The proposed proprietary name, Xarelto, is acceptable.

If you have any questions or need clarifications, please contact Linda Wu, OSE project manager, at 240-402-5120.

3.1 COMMENTS TO JANSSEN PHARMACEUTICALS, INC.

We have completed our review of the proposed proprietary name, Xarelto, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your submission, received on August 12, 2021, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. USAN Stems (https://www.ama-assn.org/about/united-states-adopted-names-approved-stems)

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html).

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [c]

[c] National Coordinating Council for Medication Error Reporting and Prevention. https://www.nccmerp.org/about-medication-errors Last accessed 10/05/2020.

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

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/

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