CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

214358Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

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

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	January 28, 2021
Application Type and Number:	(b) (4) NDA 214358
Product Name and Strength:	(b) (4) Pradaxa (dabigatran etexilate) oral pellets 20 mg per packet, 30 mg per packet, 40 mg per packet, 50 mg per packet, 110 mg per packet, 150 mg per packet
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI)
Panorama #:	2020-43806321 and 2020-43814893
DMEPA Safety Evaluator:	Stephanie DeGraw, PharmD
DMEPA Team Leader:	Hina Mehta, PharmD
DMEPA Associate Director of Nomenclature and Labeling:	Chi-Ming (Alice) Tu, PharmD

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Pradaxa, 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. BIPI did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Pradaxa (dabigatran etexilate) capsules were approved on October 19, 2010, under NDA 022512. Pradaxa capsules are indicated to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation, for the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) in patients who have been treated with a parenteral anticoagulant for 5-10 days, to reduce the risk of recurrence of DVT and PE in patients who have been previously treated, and for the prophylaxis of DVT and PE in patients who have undergone hip replacement surgery.

(b) (4)

BIPI also submitted NDA 21358 for dabigatran etexilate for the treatment of venous thromboembolic events (VTE) in pediatric patients (b) (4) 12 years of age who have been treated with a parenteral anticoagulant for at least 5 days and to reduce the risk of recurrence of VTE in pediatric patients (b) (4) 12 years of age who have been previously treated. NDA 21358 proposes a new "oral pellet" dosage form of dabigatran etexilate in the following strengths: 20 mg per packet, 30 mg per packet, 40 mg per packet, 50 mg per packet, 110 mg per packet, and 150 mg per packet.

Therefore, BIPI submitted the name, Pradaxa, for the newly proposed new dosage (b) (4) for (b) (4) NDA 214358 on November 6, 2020.

1.2 PRODUCT INFORMATION

The product information below is provided in the November 6, 2020 proprietary name submissions, the proposed Prescribing Information for (b) (4) Pradaxa pellets, and the Prescribing Information for Pradaxa capsules.

Table 1. Relevant Product Information for Pradaxa			
Product	(b) (4)	**Pradaxa (NDA 214358)**	**Pradaxa (NDA 022512)**
Initial Approval Date		Under review	October 19, 2010
Active Ingredient	dabigatran etexilate		
Indication	(b) (4)	• For the treatment of venous thromboembolic events (VTE) in pediatric patients less than 12 years of age who have been treated with a parenteral anticoagulant for at least 5 days • To reduce the risk of recurrence of VTE in pediatric patients less than 12 years of age who have been previously treated	• To reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation • For the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) in patients who have been treated with a parenteral anticoagulant for 5-10 days • To reduce the risk of recurrence of DVT and PE in patients who have been previously treated • For the prophylaxis of DVT and PE in patients who have undergone hip replacement surgery **PROPOSED*:** • For the treatment of venous thromboembolic events (VTE) in pediatric patients 8 years of age and older who have been treated with a parenteral anticoagulant for at least 5 days • To reduce the risk of recurrence of VTE in pediatric patients 8 years of age and older who have been previously treated
Route of Administration	oral		
Dosage Form	(b) (4)	Pellets	Capsules
Strength	(b) (4)	20 mg per packet	75 mg

		30 mg per packet 40 mg per packet 50 mg per packet 110 mg per packet 150 mg per packet	110 mg 150 mg
Dose and Frequency§		Weight and age-based dosing: 20 mg to (b) (4) mg twice daily	Adult dosing based on indication and CrCl: • 75 mg or 150 mg twice daily • 110 mg or 220 mg once daily Proposed pediatric dosing based on weight and (b) (4)*: 75 mg to (b) (4) mg twice daily
Preparation and Administration		Pellets should be mixed with either with soft foods or apple juice and administered orally within 30 minutes of mixing.	Swallow capsules whole with a full glass of water.
How Supplied		Each strength is supplied as 60 packets in an aluminum bag in a unit of use carton.	Each strength is supplied in a 60-count unit of use bottle and a 60-count blister package.
Storage		Store at 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]. Store in the original package to protect from moisture. Do not open the packets until ready for use. Use the PRADAXA pellets within 6 months of opening the aluminum bag containing the packets.	Bottles: Store at 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]. Once opened, the product must be used within 4 months. Keep the bottle tightly closed. Store in the original package to protect from moisture. Blisters: Store at 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

	(b) (4)		Room Temperature]. Store in the original package to protect from moisture.

***** Pediatric indications and dosing proposed under NDA 022512/S-041. This supplement is under review.

§ See Appendix B for more detailed dosage information for Pradaxa

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Pradaxa would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Non-Malignant Hematology (DNH) concurred with the findings of OPDP's assessment for Pradaxa.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) Search

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

2.2.2 Components of the Proposed Proprietary Name

BIPI did not provide a derivation or intended meaning for the proposed proprietary name, Pradaxa, 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.

2.2.3 Comments from Other Review Disciplines at Initial Review

In response to the OSE, November 23, 2020 e-mail, the Division of Non-Malignant Hematology (DNH) did not forward any comments or concerns relating to Pradaxa at the initial phase of the review.

2.2.4 Multiple Dosage Forms Under a Single Proprietary Name

We note that the newly proposed dosage (b) (4) "oral pellets" are being proposed to cover pediatric patients who cannot swallow the currently marketed

[a] USAN stem search conducted on December 16, 2020.

Pradaxa capsules. In addition to (b) (4) NDA 214358, the Sponsor submitted a Prior Approval Supplement (PAS) to NDA 022512/S-041 to propose the use of Pradaxa capsules for the treatment of VTE in pediatric patients 8 years of age and older who have been treated with a parenteral anticoagulant for at least 5 days and to reduce the risk of recurrence of VTE in pediatric patients 8 years of age and older who have been previously treated. This supplement is currently under review.

We note that the newly proposed dosage (b) (4) share the same active ingredient, indication, route of administration, and frequency as the currently approved Pradaxa capsule dosage form. Additionally, we note that the capsules and oral pellets will share strengths of 110 mg and 150 mg. Certain doses may overlap as well. Per the prescribing information submitted with the new NDAs and PAS, certain pediatric doses (e.g. a 75 mg dose) may be achieved using any (b) (4) dosage formulations. Determination of the appropriate dosage form would be made by the healthcare professional depending on the ability of the patient to swallow the available dosage formulations.

It is a common and accepted practice to have multiple dosage forms of an active ingredient managed under one proprietary name. In this case, the residual risk of confusion between the (b) (4) dosage formulations of the product may be mitigated through labels and labeling intervention.

Furthermore, we note that through our routine monitoring we have not identified any medication errors involving name confusion with the proprietary name Pradaxa. 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 Pradaxa acceptable.

2.2.5 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Non-Malignant Hematology (DNH) via e-mail on January 26, 2021. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Non-Malignant Hematology (DNH) on January 28, 2021, they stated no additional concerns with the proposed proprietary name, Pradaxa.

3 CONCLUSION

The proposed proprietary name, Pradaxa, is acceptable.

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

3.1 COMMENTS TO BOEHRINGER INGELHEIM PHARMACEUTICALS, INC.

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

If any of the proposed product characteristics as stated in your submission, received on November 6, 2020, 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.[b]
    b. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

       The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

       Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

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

When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings and provides an overall risk assessment of the proposed proprietary name.

***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.

Appendix B: Dosage and Administration Information for Pradaxa (dabigatran etexilate)

Pradaxa (dabigatran etexilate) Capsules (NDA 022512)

Recommended Dose for Adults

Indication	Dosage	
Reduction in Risk of Stroke and Systemic Embolism in Non-valvular AF	CrCl >30 mL/min:	150 mg twice daily
	CrCl 15 to 30 mL/min:	75 mg twice daily
	CrCl <15 mL/min or on dialysis:	Dosing recommendations cannot be provided
	CrCl 30 to 50 mL/min with concomitant use of P-gp inhibitors:	Reduce dose to 75 mg twice daily if given with P-gp inhibitors dronedarone or systemic ketoconazole.
	CrCl <30 mL/min with concomitant use of P-gp inhibitors:	Avoid coadministration
Treatment of DVT and PE **Reduction in the Risk of Recurrence of DVT and PE**	CrCl >30 mL/min:	150 mg twice daily
	CrCl ≤30 mL/min or on dialysis:	Dosing recommendations cannot be provided
	CrCl <50 mL/min with concomitant use of P-gp inhibitors:	Avoid coadministration
Prophylaxis of DVT and PE Following Hip Replacement Surgery	CrCl >30 mL/min:	110 mg for first day, then 220 mg once daily
	CrCl ≤30 mL/min or on dialysis:	Dosing recommendations cannot be provided
	CrCl <50 mL/min with concomitant use of P-gp inhibitors:	Avoid coadministration

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