CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208658Orig1s000

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:	April 21, 2016
Application Type and Number:	NDA 208658
Product Name and Strength:	Synjardy XR (empagliflozin and metformin HCl extended-release tablets) 5 mg/1000 mg 10 mg/1000 mg 12.5 mg/1000 mg 25 mg/1000 mg
Product Type:	Multi-ingredient
Rx or OTC:	Rx
Applicant/Sponsor Name:	Boehringer Ingelheim
Panorama #:	2016-2943931
DMEPA Primary Reviewer:	Sarah K. Vee, PharmD
DMEPA Team Leader:	Yelena Maslov, PharmD
DMEPA Deputy Director:	Lubna Merchant, PharmD, MS

Contents

1 INTRODUCTION

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

1.1 REGULATORY HISTORY

The proposed root name, 'Synjardy', for the approved immediate release product, empagliflozin and metformin HCl, was previously assessed and found acceptable in OSE Proprietary Name Review #2014-26096[1]and 2015-887595[2], dated October 20, 2014 and August 7, 2015, respectively, under NDA 206111, which was approved on August 26, 2015.

1.2 PRODUCT INFORMATION

The following is a comparison of product characteristics for Synjardy and Synjardy XR. The product information for Synjardy XR is provided in the March 2, 2016 proprietary name submission.

Table 1. Relevant Product Information for Jentadueto and Jentadueto XR		
	Synjardy (NDA 206111)	**Synjardy XR (NDA 208658)**
Approval Date	August 26, 2015	Pending
Intended Pronunciation	sin-JAR-dee	sin-JAR-dee XR
Active Ingredient	Empagliflozin and metformin HCl	Empagliflozin and metformin HCl extended-release
Indication of Use	• As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (b) (4) [redacted] (b) (4)	
Route of	Oral	

[1] Vee S. Proprietary Name Review for Synjardy (NDA 206111). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2014 OCT 20. 29 p. OSE RCM No.: 2014-26096.

[2] Vee S. Proprietary Name Memo for Synjardy (NDA 206111). Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2015 AUG 7. 29 p. OSE RCM No.: 2015-887595.

Administration		
Dosage Form	Tablets	
Strengths	5 mg/500 mg 5 mg/1000 mg 12.5 mg/500 mg 12.5 mg/1000 mg	5 mg/1000 mg 10 mg/1000 mg 12.5 mg/1000 mg 25 mg/1000 mg
Dose & Frequency	1 tablet twice daily (max 25 mg empagliflozin and 2000 mg metformin daily)	1 tablet once daily (max 25 mg empagliflozin and 2000 mg metformin)
How Supplied	Bottles of 60, 180	5 mg/1000 mg: Bottles of 60, 180 10 mg/1000 mg: Bottles of 30, 90 12.5 mg/1000 mg: Bottles of 60, 180 25 mg/1000 mg: Bottles of 30, 90
Storage	Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature]. Store in a safe place out of reach of children.	

2 RESULTS

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

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA and the Division of Metabolism and Endocrinology Products (DMEP) concurred with the findings of OPDP's assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the name.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proprietary name[3].

2.2.2 Components of the Proposed Proprietary Name

The proposed proprietary name contains two components: 1) the root name, Synjdary, and 2) the modifier XR. The Applicant indicated in their submission that the root name, Synjardy, has no derivation and the modifier 'XR' is an abbreviation for "extended release". An analysis of the proposed root name and appropriateness of the modifier is discussed in Section 2.2.6.

[3]USAN stem search conducted on March 16, 2015.

2.2.3 FDA Name Simulation Studies

Eighty-eight practitioners participated in DMEPA's prescription studies. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. The most common misinterpretation was 'i' for the 'y'. Appendix B contains the results from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, March 30, 2016 e-mail, DMEP did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.5 Medication Error Data Selection of Cases

We searched the FDA Adverse Event Reporting System (FAERS) database using the strategy listed in Table 2 (see Appendix A1 for a description of FAERS database) for name confusion errors involving ***Synjardy*** that would be relevant for this review.

Table 2. FAERS Search Strategy	
Search Date	March 16, 2016
Drug Name	Synjardy [product name]
Event (MedDRA Terms)	**DMEPA Official Proprietary Name Review Search Terms Event List:** Product name confusion (PT) Medication error (PT) Intercepted medication error (PT) Drug dispensing error (PT) Intercepted drug dispensing error (PT) Circumstance or information capable of leading to a medication error (PT)
Date Limits	August 1, 2015 to March 16, 2016

No cases were identified.

2.2.6 Analysis of the Root Name and Proposed Modifier XR

The root name, 'Synjardy', is approved for the immediate release product, empagliflozin and metformin HCl product, and has been on the market since August of 2015. The immediate-release empaglifozin and metformin HCl product, is available in 5 mg/500 mg, 5 mg/1000 mg, 12.5 mg/500 mg, and 12.5 mg/1000 mg strengths and administered twice a day. We have not identified any cases of name confusion related to the root name, Synjardy. According to the Applicant, Synjardy XR is an extended-release formulation taken once daily. The extended-release formulation will have the same strengths (5 mg/1000 mg and 12.5 mg/1000 mg), dose (1 tablet), and indication as the

immediate release product. The modifier 'XR' is used to differentiate the empagliflozin and metformin HCl extended-release formulation from the empagliflozin and metformin HCl immediate-release formulation. This modifier is commonly used for product line extensions to distinguish an extended-release formulation taken once daily from the immediate-release formulation (e.g., Janumet XR, Actoplus Met XR, or Glucophage XR). The difference in frequency of administration indicates a need to differentiate this product from the immediate-release empagliflozin and metformin HCl formulation in terms of nomenclature.

Furthermore, post-marketing medication errors have identified cases of chewing, splitting, and crushing of extended-release products. In some cases, the reporters indicate they were unaware the product was an extended-release formulation. Therefore, the addition of the modifier may minimize some of these errors.

We note that omission and oversight of a modifier is cited in literature as a common cause of medication error[4]. Postmarketing experience shows that the introduction of product line extensions result in medication errors if the modifier is omitted and the product characteristics are similar or overlap. However, the alternative to using a modifier to distinguish this product from the currently marketed products is to use a totally different root name. However, introducing a new proprietary name for this product also carries a risk of medication errors, specifically, therapeutic duplication and overdoses. These errors may have greater associated safety risks then the omission or oversight of the modifier. Therefore, for the aforementioned reasons listed, we find that the proprietary name 'Synjardy XR,' although not free from the risk of error, offers a safe approach to naming this product.

Furthermore, we recommend that the Applicant uses container labels and carton labeling as a means to differentiate the products to help minimize selection errors.

2.2.7 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to DMEP via e-mail on April 11, 2016. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DMEP on April 15, 2016, they stated no additional concerns with the proposed proprietary name, Synjardy XR.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have any questions or need clarifications, please contact Terrolyn Thomas, OSE project manager, at 240-402-3981.

3.1 COMMENTS TO THE APPLICANT

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

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[4] Lesar TS. Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8): 579-587.

If any of the proposed product characteristics as stated in your March 2, 2016 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. ***USAN Stems (http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page)***

   USAN Stems List contains all the recognized USAN stems.

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. [5]

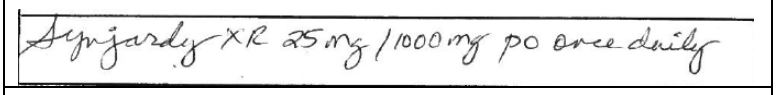
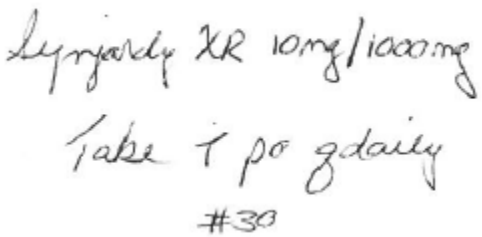
[5] National Coordinating Council for Medication Error Reporting and Prevention. http://www nccmerp.org/aboutMedErrors.html. Last accessed 10/11/2007.

Appendix A1: Description of FAERS

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. FDA's Office of Surveillance and Epidemiology codes adverse events and medication errors to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Synjardy XR Study (Conducted on 3/21/2016)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order:  Outpatient Prescription:  	Synjardy XR 10 mg/1000 mg Take 1 tab PO once daily #30

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

285 People Received Study

88 People Responded

Total	30	31	27	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
CINGARDE XR	0	1	0	1
CINJARDI XR	0	3	0	3
FINJARDI SR	0	1	0	1
FINJARVI XR	0	1	0	1
SENJARDEE SR	0	1	0	1
SENJARDI XR	0	2	0	2
SINGARDI XR	0	1	0	1
SINJARDI XR	0	6	0	6
SINJARDY XR	0	1	0	1
SINJARNI XR	0	1	0	1
SYNARDY XR	1	0	0	1
SYNBGARDI-XR	0	1	0	1
SYNDARY XR	0	1	0	1
SYNGARDI XR	0	1	0	1
SYNJARDI XR	0	8	0	8
SYNJARDY XR	27	0	26	53
SYNJARDY XR 25/100 MG	0	0	1	1
SYNJARDYXR	1	0	0	1

SYRJARDY XR	1	0	0	1
THINJARDEE XL	0	1	0	1
THINJARNEY XR	0	1	0	1

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/s/

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04/21/2016

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