

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

208026Orig1s000

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:	September 15, 2015
Application Type and Number:	NDA 208026
Product Name and Strength:	Jentaducto XR (linagliptin and metformin HCl extended-release) tablets, 5 mg/1000 mg and 2.5 mg/1000 mg
Product Type:	Multi-ingredient
Rx or OTC:	Rx
Applicant/Sponsor Name:	Boehringer Ingelheim
Panorama #:	2015-1055053
DMEPA Primary Reviewer:	Sarah K. Vee, PharmD
DMEPA Team Leader:	Yelena Maslov, PharmD

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Jentadueto 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, 'Jentadueto', for the approved immediate release product, linagliptin and metformin HCl, was previously assessed and found acceptable in OSE Proprietary Name Review #2011-3166¹, dated November 9, 2011, under NDA 201281, which was approved on January 30, 2012.

1.2 PRODUCT INFORMATION

The following is a comparison of product characteristics for Jentadueto and Jentadueto XR. The product information for Jentadueto XR is provided in the July 27, 2015 proprietary name submission.

	Jentadueto (NDA 201281)	Jentadueto XR (NDA 208026)
Approval Date	January 30, 2012	Pending
Intended Pronunciation	JEN ta doo e'-toe	JEN ta doo e'-toe XR
Active Ingredient	Linagliptin and metformin HCl	Linagliptin and metformin HCl extended-release
Indication of Use	combination product indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both linagliptin and metformin is appropriate	
Route of Administration	Oral	
Dosage Form	Tablets	
Strengths	2.5 mg/500 mg 2.5 mg/850 mg 2.5 mg/1000 mg	5 mg/1000 mg 2.5 mg/1000 mg
Dose & Frequency	1 tablet twice daily (max 2.5 mg linagliptin/1000 mg metformin twice daily)	1 tablet once daily (max 5 mg linagliptin and 2000 mg metformin)
How Supplied	60 & 180 count bottles	5 mg/1000 mg • 30 & 90 count bottles 2.5 mg/1000 mg

¹ Fava W. Proprietary Name Review for Jentadueto (NDA 201281). 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); 2011 NOV 9. 29 p. OSE RCM No.: 2011-3166.

		• 60 & 180 count bottles
Storage	Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F) [see USP Controlled Room Temperature]. Protect from exposure to high humidity. 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 name².

2.2.2 *Components of the Proposed Proprietary Name*

The proposed proprietary name contains two components: 1) the proposed root name, Jentaducto, and 2) the modifier XR. The Applicant indicated in their submission that the proposed root name, Jentaducto, 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 Sections 2.2.6 and 2.2.7 respectively.

2.2.3 *FDA Name Simulation Studies*

Sixty-nine 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 ‘G’ for the ‘J’. 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, August 21, 2015 e-mail, DMEP did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

²USAN stem search conducted on September 2, 2015.

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 *Jentadueto* that would be relevant for this review.

Table 2. FAERS Search Strategy	
Search Date	August 31, 2015
Drug Name	Jentadueto [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	January 1, 2012 to August 31, 2015

No cases were identified.

2.2.6 Analysis of Proposed Root Name

The proposed root name, ‘Jentadueto’, for the approved immediate release product, linagliptin and metformin HCl, was previously assessed and found acceptable in OSE Proprietary Name Review #2011-3166, dated November 9, 2011, under NDA 201281 and has been on the market since early 2012.

2.2.7 Analysis of Modifier XR

An immediate-release linagliptin and metformin HCl product, available in 2.5 mg/500 mg, 2.5 mg/850 mg, 2.5 mg/1000 mg strengths and administered twice a day, is currently approved. We have not identified any cases of name confusion related to the root name, Jentadueto. According to the Applicant, Jentadueto XR is an extended-release formulation taken once daily. The modifier ‘XR’ is used to differentiate the linagliptin and metformin HCl extended-release formulation from the linagliptin 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 linagliptin 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 error³. 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 than the omission or oversight of the modifier. Therefore, for the aforementioned reasons listed, we find that the proprietary name ‘Jentaducto 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.

2.2.8 Communication of DMEPA’s Analysis at Midpoint of Review

DMEPA communicated our findings to DMEP via e-mail on September 4, 2015. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from DMEP on September 8, 2015, they stated no additional concerns with the proposed proprietary name, Jentaducto 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

If any of the proposed product characteristics as stated in your July 27, 2015 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

³ Lesar TS. Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8): 579-587.

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 DNNDP. OPDP or DNNDP 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 DNNDP 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.⁴

⁴ 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. Jentaduetto XR Study (Conducted on 8/7/2015)

Handwritten Requisition Medication Order	Verbal Prescription
<p>Medication Order:</p> <div style="border: 1px solid black; padding: 5px; margin: 5px 0;"> <p><i>Jentaduetto XR 5mg/1000mg po once daily</i></p> </div> <p>Outpatient Prescription:</p> <p><i>Jentaduetto XR 2.5mg/1000mg 1 tab po QD</i></p>	<p>Jentaduetto XR 2.5 mg/1000 mg 1 tab by mouth daily</p>

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Jentaduetto XR

244 People Received Study

69 People Responded

Total	26	20	23	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
CHENTADUATO XR	0	1	0	1
CHENTEDUETO XR	0	1	0	1
CHENTODUETTO XR	0	1	0	1
GENINUENTO XR	0	1	0	1
GENTA DUETTO XR	0	1	0	1
GENTADUENTO XR	0	3	0	3
GENTADUETA XR	0	1	0	1
GENTADUETO XR	18	4	2	24
GENTADUETTO XR	0	1	0	1
GENTADUOTO XR	0	1	0	1
JENTADEUTO ER	1	0	0	1
JENTADUENTO XR	0	2	0	2
JENTADUETO SR	1	0	0	1
JENTADUETO XR	6	3	18	27
JENTADVETO XR	0	0	1	1
JENTDUETO	0	0	1	1
JENUADUETO XR	0	0	1	1

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/s/

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09/15/2015

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