CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

209210Orig1s000

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)

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Date of This Review:	March 9, 2017
Application Type and Number:	NDA 209210
Product Name and Strength:	Bydureon Bcise (exenatide extended-release) suspension, 2 mg
Product Type:	Single Ingredient, Combination Product
Rx or OTC:	Rx
Applicant/Sponsor Name:	AstraZeneca
Panorama #:	2016-12079394
DMEPA Primary Reviewer:	Ariane O. Conrad, PharmD, BCACP, CDE
DMEPA Team Leader:	Hina Mehta, PharmD
Associate Director (Acting):	Mishale Mistry, PharmD

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Bydureon Bcise, 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

Bydureon (exenatide extended release suspension) was approved on January 27, 2012 under NDA 22200. The Applicant previously submitted the proposed proprietary name, Bydureon Bcise, on August 4, 2015 under IND 107815. The Division of Medication Error Prevention and Analysis (DMEPA) found the name conditionally acceptable in OSE Review #2015-1272889,[a] dated December 2, 2015.

Thus, the Applicant has resubmitted the name, Bydureon Bcise, for review under the NDA on December 21, 2016.

1.2 PRODUCT INFORMATION

Table 1 presents relevant product information for Bydureon Bcise that AstraZeneca provided in the December 21, 2016 proprietary name submission and Bydureon.

Table 1. Relevant Product Information for Bydureon and Bydureon Bcise

	Bydureon (NDA 22200)	Bydureon Bcise (NDA 209210)
Approval Date	January 27, 2012	n/a
Intended Pronunciation	by-DUR-ee-on	by-DUR-ee-on B-cise
Active Ingredient	Exenatide extended-release	
Indication of Use	an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus	
Route of Administration	Subcutaneous	
Dosage Form	For injectable suspension	Injectable suspension
Strengths	2 mg	
Dose & Frequency	2 mg injected subcutaneously every 7 days (once weekly)	
How Supplied	Single dose tray containing 2 mg vial Single dose 2 mg pen	Pre-filled single-dose autoinjector
Storage	• Store in the refrigerator at 36°F to 46°F (2°C to 8°C), up to the	• Store in the refrigerator at 36F to 46F (2C to 8C), up the

[a] Vee S. Proprietary Name Review for Bydureon Bcise (IND 107815). 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 Dec 2. Panorama # 2015-1272889.

	expiration date or until preparing for use. • Do not freeze. • Protect from light. • Bydureon can be kept at room temperature not to exceed 77°F (25°C) for no more than a total of 4 weeks.	expiration date or until preparing for use. • Bydureon Bcise can be kept at room temperature not to exceed 86F (30C) for no more than a total of 4 weeks, if needed. • Store in original packaging and protect from light. • Bydureon Bcise must be stored flat.

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 via their January 5, 2017 email. 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[b].

2.2.2 Components of the Proposed Proprietary Name

The proposed proprietary name is comprised of a root name, Bydureon, and a modifier, Bcise. The Applicant did not provide a derivation or intended meaning for the proposed name in their submission. This product will be added to the existing product line that is comprised of Bydureon (single-dose tray containing 2 mg vial, one vial connector, one prefilled diluent syringe, and two needles [one provided as a spare]) and Bydureon Pen (each single-dose pen contains 2 mg of exenatide and diluent, and includes one needle), which are both administered subcutaneously once weekly. Both vial and pen presentations require mixing prior to administration. Bydureon Bcise is a suspension that will be available in an autoinjector presentation that does *not* require mixing prior to administration. The proposed product is also administered subcutaneously once weekly. The modifier "Bcise" is proposed to differentiate the autoinjector from the already marketed presentations of Bydureon.

In our previous review, we evaluated the need for the modifier "Bcise", the appropriateness of the modifier, and we considered if this product should utilize a different proprietary name to help

[b] USAN stem search conducted on January 10, 2017.

distinguish this product presentation from the existing product line.[a] We maintain our conclusion that the modifier "Bcise" is not misleading or vulnerable to confusion; thus, we find it acceptable for this product.

2.2.3 FDA Name Simulation Studies

Seventy-five 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. Of note, during the verbal prescription study, four participants misinterpreted the modifier "Bcise" as B5, which could be a shortened abbreviated name for vitamin B5. However, it is unlikely that this misinterpretation would occur in practice due to the product differences between vitamin B5 (available as pantothenic acid 500 mg tablet administered orally for vitamin B deficiency) and Bydureon Bcise (injectable suspension administered once weekly for type 2 diabetes). Thus, we find it unlikely this modifier, used as proposed with the root name Bydureon, will cause confusion with vitamin B5.

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 January 5, 2017 e-mail, the Division of Metabolism and Endocrinology Products (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 ***Bydureon*** that would be relevant for this review.

Table 2. FAERS Search Strategy	
Search Date	January 10, 2017
Drug Name	Bydureon [product name]
Event (MedDRA Terms)	**DMEPA Official PNR Name Confusion Search Terms Event List:** Preferred Terms: CIRCUMSTANCE OR INFORMATION CAPABLE OF LEADING TO MEDICATION ERROR DRUG ADMINISTRATION ERROR) DRUG DISPENSING ERROR DRUG PRESCRIBING ERROR INTERCEPTED DRUG DISPENSING ERROR INTERCEPTED DRUG PRESCRIBING ERROR

	INTERCEPTED MEDICATION ERROR MEDICATION ERROR PRODUCT NAME CONFUSION TRANSCRIPTION MEDICATION ERROR Lower Level Terms: INTERCEPTED PRODUCT SELECTION ERROR INTERCEPTED WRONG DRUG PRODUCT SELECTED INTERCEPTED WRONG DRUG SELECTED PRODUCT SELECTION ERROR WRONG DEVICE DISPENSED WRONG DRUG ADMINISTERED WRONG DRUG DISPENSED WRONG DRUG PRESCRIBED WRONG DRUG PRODUCT SELECTED WRONG DRUG SELECTED WRONG PRODUCT SELECTED
Date Limits	September 1, 2015-January 1, 2017

Each report was reviewed for relevancy and duplication. The NCC MERP Taxonomy of Medication Errors was used to code the case outcome and error root causes when provided by the reporter.

After individual review, 113 reports were not included in the final analysis, as they did not relate to name confusion.

Following exclusions, the search yielded 24 relevant cases. Twenty cases described product confusion between Bydureon vial/syringe and pen presentations during dispensing because the prescriber did not specify the product presentation on the medication order or the pharmacist selected the wrong product presentation. We note that both preparations of Bydureon are marketed under the same name, which may have contributed to these types of errors. Thus, the addition of a modifier should distinguish this new product from the currently marketed preparations and help to mitigate these types of errors.

Our search also identified one case of duplicate therapy with Byetta and Bydureon and three cases describing wrong drug errors. The report of product duplication described purposeful prescribing of Bydureon as add-on therapy to current Byetta therapy; therefore, we determined that this case describes intentional duplication of therapy. Two of the three cases reporting wrong drug errors reported that the "wrong medication" was dispensed to a patient but the reports did not provide enough details to determine if the wrong Bydureon product was dispensed or if the patient received a completely different drug product. The third case described a dispensing error; Bydureon was dispensed instead of the intended product, Trulicity

(dulaglutide). However, the case details did not indicate that the error was related to name confusion.

See Appendix A2 for more information.

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Metabolism and Endocrinology Products (DMEP) via e-mail on March 2, 2017. At that time, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DMEP on March 9, 2017, they stated no additional concerns with the proposed proprietary name, Bydureon Bcise.

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, Bydureon Bcise, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your December 21, 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.[c]

b. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/or outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail.

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

The voice mail messages are then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants record their interpretations of the orders which are recorded electronically.

c. 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.

   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.

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 A2: FAERS Search Results

Reported Error	# of Cases	Case Description and Reported Root Cause(s)/Contributing Factors
Bydureon vial/syringe dispensed when Bydureon Pen prescribed	10	• n=8: Prescription dispensed as the vial/syringe instead of the pen the patient was expecting. Reports unclear why the wrong product formulation was dispensed. • n=1: Vial/syringe preparation dispensed when the prescription specified the pen. Pharmacist was unfamiliar with the pen preparation. • n=1: Vial/syringe dispensed in lieu of the pen due to pharmacy availability.
Bydureon Pen dispensed when Bydureon vial/syringe prescribed	10	• n=7: Prescription dispensed as the pen instead of the vial/syringe the patient was expecting. These patients were using the vial/syringe preparation prior to the unexpected switch to the pen by the pharmacy. Reports unclear why the product formulation was changed. • n=2: Pen dispensed in lieu of the vial/syringe due to pharmacy availability. • n=1: Pen dispensed based on health insurance drug formulary requirements.

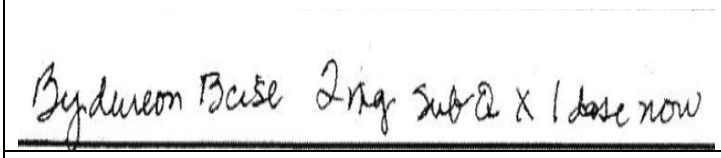
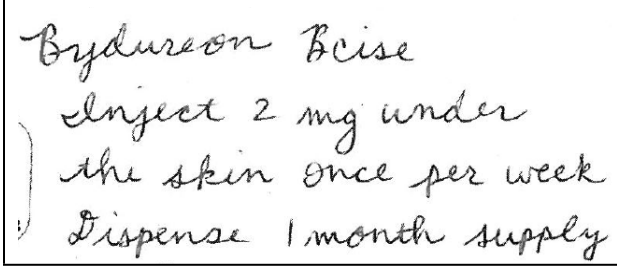
Wrong drug dispensed	3	• n=2: Reports of wrong drug dispensed and dose omission but no further information provided. • n=1: Patient prescribed Trulicity (dulaglutide) and received Bydureon. No description of why but the patient experienced side effects associated with Bydureon therapy and missed doses of Trulicity.
Duplicate therapy with Byetta and Bydureon	1	• n=1: Patient already on Byetta prescribed Bydureon as additional therapy. Patient experienced hypoglycemia but report is unclear if that is due to the duplicate therapy or the patient's other diabetes medications.

FAERS Case #	**Version**	**Manufacturer Control #**
11466019	1	US-ASTRAZENECA-2015SE34503
11805111	1	US-ASTRAZENECA-2013SE80010
11869809	1	US-ASTRAZENECA-2015SF28154
11883645	2	US-ASTRAZENECA-2015SF06025
11912646	1	US-ASTRAZENECA-2016SE01870
12060551	1	US-ASTRAZENECA-2013SE42384
12160909	2	US-ASTRAZENECA-2008BM03453
12234746	1	US-ASTRAZENECA-2016SE26819
12298074	1	US-ASTRAZENECA-2016SE42071
12315158	1	US-ASTRAZENECA-2016SE32796
12354315	1	US-ASTRAZENECA-2016SE35889
12462407	1	US-ASTRAZENECA-2016SE61198
12581403	2	US-ASTRAZENECA-2014SE19965
12662296	1	US-ASTRAZENECA-2016SE73999
12780346	1	US-ASTRAZENECA-2016SE98627
12781946	1	US-ASTRAZENECA-2016SE41933

12805560	2	US-ASTRAZENECA-2016SF00684
12863859	1	US-ASTRAZENECA-2016SF07455
12891376	2	US-ASTRAZENECA-2008BM04124
12956857	2	US-ASTRAZENECA-2016SF14003
12962706	1	US-ASTRAZENECA-2016SF18648
12966587	1	US-ASTRAZENECA-2016SF23209
12978466	1	US-ASTRAZENECA-2016SF22954
13035087	1	US-ASTRAZENECA-2007BM11986

Appendix B: Prescription Simulation Samples and Results

Figure 1. Bydureon Bcise Study (Conducted on January 13, 2017)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order:  	Bydureon Bcise Inject 2 mg under the skin once per week Dispense 1 month supply
Outpatient Prescription:  	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

Study Name: Bydrueon BCise
As of Date 1/27/2017

297 People Received Study
75 People Responded

Study Name: Bydrueon BCise

Total	32	19	24	
INTERPRETATION	**OUTPATIENT**	**VOICE**	**INPATIENT**	**TOTAL**
BIDERIAN BESIDE	0	1	0	1
BIDURIAN	0	3	0	3
BIDURIAN ???	0	1	0	1
BIDURIAN B SITE	0	1	0	1
BIDURIAN B VITE	0	1	0	1
BIDURIAN B5	0	1	0	1
BIDURIANI B5 (?)	0	1	0	1
BIDURIEN	0	1	0	1
BIDURION	0	1	0	1
BYDIARIAN BFITE	0	1	0	1
BYDUREAN B-SITE	0	1	0	1
BYDUREON	0	0	1	1
BYDUREON B5	0	1	0	1
BYDUREON BASE	0	0	7	7
BYDUREON BCISE	29	0	13	42
BYDUREON BEISE	3	0	1	4
BYDUREON BESITE	0	1	0	1
BYDUREON B-SCYTHE	0	1	0	1
BYDUREON BUSE	0	0	1	1
BYDURIAN B SITE	0	1	0	1
BYDURIAN B5	0	1	0	1
BYDURIAN BASE	0	0	1	1
BYDURIAN B-PHYTE	0	1	0	1

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/s/

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