CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Date:	October 26, 2011
Application Type/Number:	NDA 022200
Through:	Zachary Oleszczuk, Pharm.D., Team Leader Carol Holquist, R.Ph., Director Division of Medication Error Prevention and Analysis
From:	Manizheh Siahpoushan, Pharm.D., Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name and Strength:	Bydureon (Exenatide Extended-release) Injectable suspension 2 mg per vial
Applicant/sponsor:	Amylin
OSE RCM #:	2011-3137

CONTENTS

Reference ID: 3034831

1 INTRODUCTION

This review evaluates the proposed proprietary name, Bydureon, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The proposed product characteristics are provided in section 1.2 below.

1.1 REGULATORY HISTORY

This review responds to a request from Amylin Pharmaceuticals, dated August 17, 2011, for a safety and promotional assessment of the proposed proprietary name, Bydureon (NDA 022200). DMEPA reviewed the proposed name during the IND phase and found it acceptable in OSE review #2008-687 and 2009-2193, dated February 2, 2010. In that review, DMEPA also conducted a dual proprietary name risk assessment of the name Bydureon because Exenatide is currently marketed as Byetta for the same indication for use, but with different dosage form and frequency of administration. DMEPA's evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of the review on February 2, 2010. The February 2, 2010 submission also included an independent trademark safety evaluation by Med-ERRS, two separate FMEAs conducted by DSI (dated October 13, 2008) and Med-ERRS (dated March 21, 2009), as well as container labels, carton labeling, Prescribing Information, Patient Instructions for Use, and Medication Guide. which were reviewed by DMEPA in OSE review #2009-2211, dated February 25, 2010.

Additionally, the Applicant submitted revised container labels, carton labeling, prescribing Information, Patient Instructions for Use, and Medication Guide on July 28, 2011which will be reviewed under a separate cover in OSE review #2011-2841.

1.2 PRODUCT CHARACTERISTICS

Bydureon is a glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Bydureon is an extended-release formulation of Exenatide. The recommended dose is 2 mg administered subcutaneously once weekly, at any time of day, with or without meals. Bydureon is supplied in cartons of 4 single-dose kits for use. Each single-dose kit contains: One vial containing 2 mg Exenatide (as a white to off-white powder), one prefilled syringe delivering 0.65 mL diluent, one vial connector, and two custom needles (23G, 5/16") specific to this delivery system (one is a spare needle). Bydureon should be administered immediately after suspension of the powder into the diluent. Bydureon should be stored in the refrigerator up to the expiration date or until preparing for use

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

DDMAC determined that the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Metabolism and Endocrinology Products (DMEP) concurred with the findings of DDMAC's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following information is considered in the safety assessment of the proposed name.

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2.2.1 United States Adopted Names (USAN) SEARCH

The United States Adopted Name (USAN) stem search conducted on August 25, 2011, identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The proposed name is a single word that does not contain any components (i.e., modifier, dosage form, frequency, indications, etc.) that can contribute to medication error.

2.2.3 External Proprietary Name Risk Assessment

An external name risk assessment conducted by Med-ERRS, dated November 2007 for the assessment of Bydureon Look-alike and/or sound-alike potential, as well as the Failure Mode and Effects Analysis (FMEA) of naming convention conducted by DSI (dated October 13, 2008) and Med-ERRS (dated March 2009) were reviewed and analyzed by DMEPA in OSE review #2008-687 and #2009-2193, dated February 2, 2010.

2.2.4 FDA Name Simulation Studies

A total of 25 practitioners responded to the prescription analysis studies. None of the practitioners identified the name as a currently marketed drug product. Eight practitioners (n=8) in the inpatient and outpatient studies interpreted the name correctly as Bydureon. The remainder of the respondents (n=17) misinterpreted the drug name. In the verbal studies, misinterpretations occurred primarily because the letter 'y' sound was misinterpreted as the letter 'i' and the letter 'e' sound was misinterpreted as the letter 'i' when transcribed. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.5 Comments From Other Review Disciplines

In response to OSE e-mail, August 25, 2011, the Division of Metabolism and Endocrinology Products (DMEP) did not forward any comments or concerns relating to the proposed name at the initial phase of the name review.

2.2.6 Failure Mode and Effects Analysis of Similar Names

Table 1 lists the names identified to have potential orthographic, phonetic, or spelling similarity to the proposed proprietary name, Bydureon (see Appendix B). These names were identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD and Other Disciplines)

Look Similar		**Look and Sound Similar**	
Name	***Source***	***Name***	***Source***
Roferon	Safety Evaluator	Byetta	EPD Panel
Pylera	Safety Evaluator	Benuron	Safety Evaluator

Look Similar		Look and Sound Similar	
Name	***Source***	***Name***	***Source***
Hycodan	Safety Evaluator	BiDil	Safety Evaluator
Blocadren	Safety Evaluator	(b) (4)***	Safety Evaluator
Hydrea	Safety Evaluator	Bupropion	EPD Panel
Budesonide	EPD Panel	Budeprion SR or XL	EPD Panel
Anteron	Safety Evaluator	Duraclon	EPD Panel
Hylenex	Safety Evaluator	(b) (4)***	Safety Evaluator
Zemuron	Safety Evaluator	(b) (4)***	Safety Evaluator
Biperiden	Safety Evaluator	Bydureon	Safety Evaluator
Fuzeon	Safety Evaluator		
Bentyron	Safety Evaluator		
Ridaura	Safety Evaluator		
Zydone	Safety Evaluator		
Beheparon	Safety Evaluator		
Adheron	Safety Evaluator		
Hyalase	Safety Evaluator		
Iomeron	Safety Evaluator		
Byosan	Safety Evaluator		
Thydron	Safety Evaluator		
Bydaxin	Safety Evaluator		
Pydirone	Safety Evaluator		

*** This document contains proprietary and confidential information that should not be released to the public.

Look Similar		Look and Sound Similar	
Name	***Source***		
Kybernin P	Safety Evaluator		
(b) (4) ***	Safety Evaluator		
*	Safety Evaluator		
Buclizine	EPD Panel		
Bydramine	Safety Evaluator		
Vytorin	Safety Evaluator		
Enduron	EPD Panel		
Bystolic	EPD Panel		
Eryderm	Safety Evaluator		
Byclomine	Safety Evaluator		
Lysodren	Safety Evaluator		
Betaseron	Safety Evaluator		
Rynatan	EPD Panel		
Hydramine	EPD Panel		
Bupleurum	EPD Panel		
Bupleuri	EPD Panel		

Our analysis of the 48 names contained in Table considered the information obtained in the previous sections along with their product characteristics. We determined all 48 names will not pose a risk for confusion as described in Appendices D and E.

DMEPA communicated these findings to the Division of Metabolism and Endocrinology via e-mail on September 1, 2011. At that time we requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Metabolism and Endocrinology Products on October 26, 2011 the Division had no additional concerns with the proposed proprietary name, Bydureon.

*** This document contains proprietary and confidential information that should not be released to the public.

3 CONCLUSIONS

DMEPA concludes the proposed proprietary name, Bydureon is not promotional. Additionally, DMEPA did not identify any new safety concerns regarding the proposal to use a dual proprietary name for this product that was not considered during our previous review. Thus, although, the safety review of the name indicates that use of a dual name for this product carries some risk of confusion and error as does having the root name 'Byetta plus a modifier', we find Bydureon is acceptable because the use of the same prefix 'By-' in both proprietary names Bydureon and Byetta may help increase practitioner awareness that both products contain the same active ingredient, there is less risk for modifier omission, and the dual name may help increase awareness that Bydureon and Byetta are administered differently (different frequency of administration). However, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

If approval of the NDA is delayed beyond 90 days from the date of this review, the proprietary name must be re-reviewed prior to the new approval date.

6 REFERENCES

1. Micromedex Integrated Index (http://csi.micromedex.com)

Micromedex contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion.

3. Drug Facts and Comparisons, online version, St. Louis, MO (http://factsandcomparisons.com)

Drug Facts and Comparisons is a compendium organized by therapeutic course; it contains monographs on prescription and OTC drugs, with charts comparing similar products.

4. The Document Archiving, Reporting, and Regulatory Tracking System (DARRTS)

DARRTS is a government database used to track individual submissions and assignments in review divisions.

5. 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.

6. Drugs@FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)

Drugs@FDA contains most of the drug products approved 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, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

7. Electronic online version of the FDA Orange Book (http://www.fda.gov/cder/ob/default.htm)

The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

8. U.S. Patent and Trademark Office (http://www.uspto.gov)

USPTO provides information regarding patent and trademarks.

9. Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)

Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also provides a keyword search engine.

10. Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com)

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

11. Natural Medicines Comprehensive Databases (www.naturaldatabase.com)

Natural Medicines contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

12. Access Medicine Database (http://www.accessmedicine.com/drugs.aspx)

Access Medicine contains full-text information from approximately 60 medical titles: it includes tables and references. Among the database titles are: Goodman and Gilman's The Pharmacological Basis of Therapeutics, Current Medical Diagnosis and Treatment, Tintinalli's Emergency Medicine, and Hurst's the Heart.

13. USAN Stems (http://www.ama-assn.org/ama/pub/category/4782.htmL)

USAN Stems List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

Red Book contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

15. Lexi-Comp (www.lexi.com)

Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

16. Medical Abbreviations Book

Medical Abbreviations Book contains commonly used medical abbreviations and their definitions.

17. LabelDataPlus Database (http://www.labeldataplus.com/index.php?ns=1)

LabelDataPlus database covers a total of 36773 drug labels. This includes Human prescription drug labels as well as Active Pharmaceutical Ingredients (APIs), OTC (Application and Monograph) drugs, Homeopathic drugs, Unapproved drugs, and Veterinary drugs.

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. 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. [1]

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [2] DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and

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

[2] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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monitoring the impact of the medication.[3] DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly in spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

Type of similarity	**Considerations when searching the databases**		
	Potential causes of drug name similarity	*Attributes examined to identify similar drug names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication

[3] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

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	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the DMEPA staff to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA Prescription Analysis Studies

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 the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. 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 send their interpretations of the orders via e-mail to DMEPA.

4. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary name and 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 DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND or 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 concur/not concur with DMEPA's final decision.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[4] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug

[4] Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

> ***"Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?"***

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

> ***"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"***

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Risk Assessment:

a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Sponsor. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Sponsor can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval. . (See Section 4 for limitations of the process).

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance,

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In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

Appendix B: Letters with possible orthographic or phonetic misinterpretation

Letters	**Scripted may appear as**	**Spoken may be interpreted as**
Capital 'B'	'R', 'D', 'P', 'K', 'Z', 'H', 'E'	'P', 'D', 'V'
Lower case 'b'	'l', 'h', 'k'	'p', 'v', 'd'
Lower case 'y'	'f', 'p', 'u', 'v', 'x', 'Z'	'e', 'i', 'u'
Lowe case 'd'	'cl', 'ci', 'a'	'b', 't'
Lower case 'u'	'n', 'y', 'v', 'w', Any Vowel	Any Vowel
Lower case 'r'	's', 'n', 'e', 'v'	'wr'
Lower case 'e'	'a', 'i', 'l', 'o', 'u', 'p'	Any Vowel
Lower case 'o'	'a', 'u', 'c', 'e'	'oh'
Lower case 'n'	'm', 'u', 'x', 'r', 'h', 's'	'dn', 'gn', 'kn', 'mn', 'pn'

Appendix C: FDA Prescription Study for Bydureon (8/26/11)

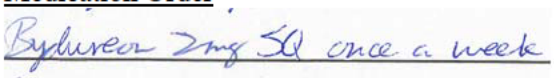
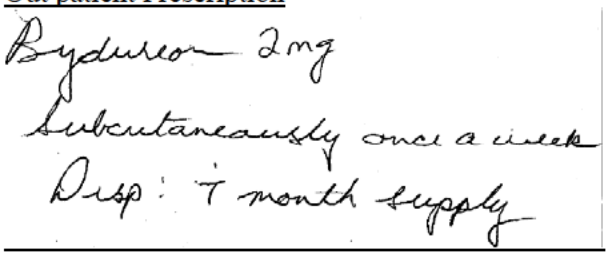
Handwritten Requisition Medication Order	Verbal Prescription
Medication Order 	Bydureon 2 mg subcutaneously once a week 1 month supply
Out patient Prescription 	

Table 1: Responses to prescription study (25 responses on 8/30/11)

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Bydriveon	Bydrueon	Bidureon
Bydriveor	Bydureo	Bidurion
Bydureon	Bydureon	Bidurion
Bydureon	Bydureon	Bidurion
Bydureon	Bydureon	Bidurion
Byduveon	Bydureon	Bydurion
Byduveon	Bydureon	Bydurion
Byhiveon		
Byhiveor		
Byluveon		
Byluvreo		

Appendix D: Names eliminated from further evaluation for reasons listed below

	Proprietary Name	Similarity to Bydureon	Reason Eliminated
1	Roferon	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
2	Pylera	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
3	Hycodan	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
4	Blocadren	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
5	Hydrea	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
6	Budesonide	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
7	Anteron	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
8	Hylenex	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
9	Zemuron	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
10	Biperiden	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
11	Fuzeon	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
12	Bentyron	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.

13	Ridaura	Look/Sound	Name lacks convincing orthographic or phonetic similarities to Bydureon.
14	Zydone	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
15	Byetta	Look/Sound	Name lacks convincing orthographic or phonetic similarities to Bydureon.
16	Beheparon	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
17	Adheron	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
18	Benuron	Look/Sound	Name lacks convincing orthographic or phonetic similarities to Bydureon.
19	BiDil	Look/Sound	Name lacks convincing orthographic or phonetic similarities to Bydureon.
20	Hyalase	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
21	Iomeron	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
22	Byosan	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
23	Thydron	Look	Name lacks convincing orthographic or phonetic similarities to Bydureon.
24	Bydaxin	Look	Proprietary name trademarked in Japan.

25	Pydirone	Look	Product withdrawn by Commissioner in June, 1977, with no generics available according to the Decision Support System (DSS) which was replaced by DARRTS database. Name was not transferred to DARRTS or found in any other databases.
26	(b) (4) ***	Look/Sound	Proprietary name withdrawn in (b) (4), and was never marketed (found in the DARRTS database).
27	Kybernin P	Look	Orphan drug designee not approved by the Agency.
28	(b) (4) ***	Look/Sound	(b) (4) .
29	Bydureon	Look/Sound	Pending trademarked name by the Applicant in foreign countrie (b) (4)
30	(b) (4) ***	Look/Sound	(b) (4)
31	(b) (4) ***	Look	(b) (4)

*** This document contains proprietary and confidential information that should not be released to the public

32	(b) (4)	Look	(b) (4)
33	Buclizine	Look	An oral anticholinergic for the control of nausea, vomiting, and dizziness associated with motion sickness; approved by the FDA in 1954. Drug has been discontinued in the United States.

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

PROPOSED NAME: Bydureon (Exenatide Extended-release) Injectable Suspension		**STRENGTH:** **2 mg**	**USUAL DOSE:** **2 mg subcutaneously once weekly.**
FAILURE MODE: Name Confusion		**CAUSES:** (Potential reasons for name confusion that could lead to medication error)	**PREVENTION OF FAILURE MODE** (Reasons why the risk of medication error is minimized)
1	Bydramine (Diphenhydramine Hydrochloride) Oral solution 12.5 mg/5 mL (Discontinued, but generic equivalents are available.) Usual Dose 12.5 mg to 25 (1 to 2 teaspoonful) mg by mouth every 4 to 6 hours.	Orthographic Both names share the letter string 'Byd-'. The letter string '-re-' in Bydureon may appear similar to the letter string '-ra-' in Bydramine when scripted. Additionally, both names share the letter 'n' in the 8th position. Strength Single strength Numerical Overlap in the Usual Dose 2 mg vs. 2 teaspoonful	Route of Administration Subcutaneous vs. oral Dosage Form Injectable suspension vs. oral syrup Frequency of Administration Weekly vs. every 4 to 6 hours.

*** This document contains proprietary and confidential information that should not be released to the public

2	Bupropion (Bupropion) Tablets 75 mg, 100 mg (Bupropion) Extended-release Tablets 150 mg, 300 mg <u>Usual Dose</u> Immediate release: 300 mg by mouth daily, given 3 times daily. Begin at 200 mg/day, given as 100 mg twice daily. Extended-release: 300 mg by mouth daily, given once daily. Begin at 150 mg/day, given as a single daily dose.	<u>Orthographic/Phonetic</u> The letter strings 'By-' and '-eon' in Bydureon may appear similar to the letter strings 'Bu-' and '-ion' in Bupropion when scripted. Phonetically, both names consist of 4 syllables and share a similar sound in the last syllable ('yon'). <u>Partial Overlap in the Frequency of Administration</u> Once	<u>Orthographic/Phonetic</u> One downstroke ('y') and two upstrokes ('B', 'd') in Bydurion vs. two downstrokes ('p' and 'p') and one upstroke ('B') in Bupropion. Phonetically, the two names do not share similar sounds in the first 3 syllables of the names. <u>Route of Administration</u> Subcutaneous vs. oral <u>Dosage Form</u> Injectable suspension vs. tablets <u>Strength</u> 2 mg vs. 75 mg, 100 mg, 150 mg, 300 mg .
3	Budeprion SR (Bupropion) Extended-release Tablets 100 mg, 150 mg Budeprion XL (Bupropion) Extended-release Tablets 300 mg <u>Usual Dose</u> 300 mg by mouth per day, given once daily. Begin at 150 mg/day, given as a single daily dose.	<u>Orthographic/Phonetic</u> The letter strings 'Bydu-' and '-eon' in Bydureon may appear similar to the letter strings 'Bude-' and '-ion' in Budeprion SR (or XL) when scripted. Phonetically, both names share 4 syllables (if the modifiers 'SR' and 'XL' are omitted) and share a similar sound in the fourth syllable ('yon'). <u>Partial Overlap in the Frequency of Administration</u> Once	Orthographic/Phonetic The position of the down stroke 'y' in Bydureon (2^{nd} position) is different than the position of the downstroke 'p' in Budeprion SR (or XL) (5^{th} position) and may help differentiate the two names. Additionally, if included, the modifiers 'SR' and 'XL' may also help differentiate the two names. Phonetically, the first 3 syllables of Bydureon and Budeprion SR (or XL) sound different. <u>Route of Administration</u> Subcutaneous vs. oral <u>Dosage Form</u> Injectable suspension vs. tablets <u>Strength</u> 2 mg vs. 100 mg, 150 mg, 300 mg <u>Frequency of Administration</u> Once weekly vs. daily, twice or three times daily.

4	Vytorin (Ezetimibe/Simvastatin) Tablets 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg Usual Dose 10 mg/10 mg to 10 mg/80 mg (or one tablet) by mouth daily.	Orthographic The letter string 'Bydure-' in Bydureon may appear similar to the letter string 'Vytori-' in Vytorin when scripted (if the letter 'B' in Bydureon is scripted in the lower case). Additionally, both names share the letter 'n' as the last letter. Partial Overlap in the Frequency of Administration Once	Orthographic The name Bydureon may appear longer than the name Vytorin when scripted due to the extra letter 'o' in Bydureon. Route of Administration Subcutaneous vs. oral Dosage Form Injectable suspension vs. tablets Strength 2 mg vs. 10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg/80 mg Usual Dose 2 mg vs one tablet
5	Enduron (Methyclothiazide) Tablets 2.5 mg, 5 mg Usual Dose 2.5 mg to 5 mg by mouth once daily.	Orthographic/Phonetic The letter 'B' in Bydureon may appear similar to the letter 'E' in Enduron when scripted. Additionally, both names share the letter strings '-dur-' and '-on'. Phonetically, the two names share the same sound ('du') in the second syllable. Additionally, the last syllable of both names ends with 'on'. Partial Overlap in the Frequency of Administration Once	Orthographic/Phonetic One downstroke 'y' in Bydureon vs. no downstrokes in Enduron. Phonetically, there are 4 syllables in the name Bydureon vs. 3 syllables in the name Enduron. Additionally, the first syllable of the two names sounds different. Route of Administration Subcutaneous vs. oral Dosage Form Injectable suspension vs. tablets Strength 2 mg vs. 2.5 mg and 5 mg

6	Bystolic (Nebivolol) Tablets 2.5 mg, 5 mg, 10 mg, 20 mg Usual Dose 2.5 mg to 10 mg by mouth once daily.	Orthographic Both names consist of eight letters and share the letter string 'By-'. Additionally, the letter strings '-du-' and '-eo-' in Bydureon may appear similar to the letter strings '-to-' and '-ic' in Bystolic when scripted. Possible Overlap in the Strength 2 mg vs. 20 mg Partial Overlap in the Frequency of Administration Once Possible Numerical Overlap in the Usual Dose 2 mg vs. 20 mg	Orthographic Two upstrokes in Bydureon vs. three upstrokes in Bystolic. Route of Administration Subcutaneous vs. oral Dosage Form Injectable suspension vs. tablets
7	Eryderm (Erythromycin) Topical Solution 2% Usual Dose Apply to the affected area(s) in the morning and evening.	Orthographic The letter 'B' in Bydureon may appear similar to the letter 'E' in Eryderm when scripted. Additionally, the letter string '-ydur-' in Bydureon may appear similar to the letter string '-yder-' in Eryderm when scripted. Strength Single strength Frequency of Administration Once (Eryderm may be applied once)	Route of Administration Subcutaneous vs. topical Dosage Form Injectable suspension vs. topical solution Frequency of Administration Once weekly vs. twice daily Usual Dose 2 mg vs. apply to the affected area

8	Byclomine (Dicyclomine Hydrochloride) Tablets, 20 mg Usual Dose 160 mg by mouth daily, in 4 divided doses (or 2 tablets by mouth 4 times daily).	Orthographic The name Bydureon may appear similar to the letter string 'Byclomin-' in Byclomine when scripted. Strength Single strength Possible Overlap in the Frequency of Administration Once Numerical Overlap in the Usual Dose 2 tablets	Route of Administration Subcutaneous vs. oral Dosage Form Injectable suspension vs. tablets Additionally, according to the usage database, the product is not prescribed under the name Byclomine.
9	Lysodren (Mitotane) Tablets 500 mg Usual Dose 2 grams to 10 grams by mouth daily in divided doses, either 3 or 4 times daily.	Orthographic Both names consist of eight letters, share the letter string '-re-', and end with the letter 'n'. Additionally, the letter string 'By-' in Bydureon may appear similar to the letter string 'Ly-' in Lysodren when scripted. Also, the fourth letter 'u' in Bydureon and the fourth letter 'o' in Lysodren may appear similar when scripted. Strength Single strength Possible Overlap in the Frequency of Administration Once Numerical Overlap in the Usual Dose 2 mg vs. 2 grams	Orthographic The position of the upstroke 'd' in Bydureon (3^{rd} position) is different than Lysodren (5^{th} position) and may help differentiate the two names. Route of Administration Subcutaneous vs. oral Dosage Form Injectable suspension vs. tablets

10	Betaseron (Iterferon Beta-1b) Powder for Injection 0.3 mg Usual Dose 250 mcg subcutaneously every other day (after a titration schedule of 0.0625 mg x 2 weeks, 0.125 mg x 2 weeks, 0.187 mg x 2 weeks).	Orthographic Both names begin with the letter 'B' and end with the letter string '-on'. Additionally, the letter string '-dure-' in Bydureon may appear similar to the letter string '-tase-' in Betaseron when scripted. Route of Administration Subcutaneous Overlapping Dosage Form Injectable suspension Strength Single strength	Orthographic The downstroke 'y' in Bydureon may help differentiate the two names. Frequency of Administration Once weekly vs. every other day. Usual Dose 2 mg vs. a titration schedule leading to maintenance dose of 250 mcg (0.25 mg).
11	Rynatan (Phenylephrine Tannate and Chlorpheniramine Tannate) Tablets 25 mg/9 mg Usual Dose One or two tablets by mouth every 12 hours.	Orthographic The letter string 'By-' and '-on' in Bydureon may appear similar to the letter stings 'Ry-' and '-an' in Rynatan when scripted. Additionally, the fourth letter 'u' in Bydureon may appear similar to the fourth letter 'a' in Rynatan when scripted. Strength Single strength Numerical Overlap in the Usual Dose 2 mg vs. 2 tablets	Orthographic The position of the upstroke 'd' in Bydureon (3^{rd} position) is different than the position of the upstroke 't' in Rynatan (5^{th} position) which may help differentiate the two names. Route of Administration Subcutaneous vs. oral Dosage Form Injectable suspension vs. tablets Frequency of Administration Once weekly vs. every 12 hours.
12	Hydramine (Diphenhydramine Hydrochloride) Oral syrup 12.5 mg/5 mL (Discontinued, but different generic equivalents are available) Usual Dose 12.5 mg to 50 mg every 4 to 6 hours. Do not exceed 300 mg in 24 hours.	Orthographic The letter strings 'Bydur-' and '-on' in Bydureon may appear similar to the letter strings 'Hydra-' and '-in-' in Hydramine when scripted. Strength Single strength Possible Numerical Overlap in the Usual Dose 2 mg vs. 2 teaspoonfuls	Route of Administration Subcutaneous vs. oral Dosage Form Injectable suspension vs. oral syrup Frequency of Administration Once weekly vs. every 4 to 6 hours. Additionally, the product is discontinued and we can not find evidence that this product is prescribed under the name Hydramine.

13	Duraclon (Clonidine Hydrochloride) Solution for injection 100 mcg/mL, 500 mcg/mL <u>Usual Dose</u> The recommended starting dose for continuous epidural infusion is 30 mcg/hr.	<u>Orthographic/Phonetic</u> Both names consist of eight letters and end with the letter string '-on'. Additionally, the letter string 'By-' may appear similar to the letter string 'Du-' in Duraclon when scripted. The fourth letter 'u' and the sixth letter 'e' in Bydureon may appear similar to the fourth letter 'a' and the sixth letter 'l' in Duraclon when scripted. <u>Overlap in the Route of Administration</u> Subcutaneous vs. epidural <u>Dosage Form</u> Injectable	<u>Orthographic</u> The downstroke 'y' and the different position of the upstroke'd' (3rd position) in Bydureon (vs. the upstroke 'l' in the sixth position in Duraclon) may help differentiate the two names. <u>Strength</u> 2 mg vs. 100 mcg/mL and 500 mcg/mL <u>Frequency of Administration</u> Once weekly vs. continuous infusion <u>Usual dose</u> 2 mg vs. 30 mcg/hr
14	Bupleurum (Name found in the Natural Medicines database-used for fever, flu, common cold, cough, fatigue, headache, and liver disorders-available on Amazon.com) <u>Usual Dose</u> 1.5 to 6 grams by mouth daily.	<u>Orthographic</u> The letter strings 'By-' and '-dureon' in Bydureon may appear similar to the letter strings 'Bu-' and '-leurum' in Bupleurum when scripted. <u>Strength</u> Single strength <u>Possible Overlap in the Usual Dose</u> 2 mg vs. 2 grams	<u>Route of Administration</u> Subcutaneous vs. oral <u>Dosage Form</u> Injectable suspension vs. tablets Additionally, according to the usage data, this herbal remedy has never been prescribed.
15	Bupleuri (Bupleurum) (Name found in the Natural Medicines database-used for fever, flu, common cold, cough, fatigue, headache, and liver disorders-available on Amazon.com) <u>Usual Dose</u> 1.5 to 6 grams by mouth daily.	<u>Orthographic</u> Both names consist of eight letters. Additionally, the letter strings 'By-' and '-dureo' in Bydureon may appear similar to the letter strings 'Bu-' and '-leuri' in Bupleuri when scripted. <u>Strength</u> Single strength <u>Possible Overlap in the Usual Dose</u> 2 mg vs. 2 grams	<u>Orthographic</u> Although both names consist of 8 letters, the name Bydureon may appear longer when scripted because of the letter string 'on' at the end of the name. <u>Route of Administration</u> Subcutaneous vs. oral <u>Dosage Form</u> Injectable suspension vs. tablets Additionally, we can not find evidence that this herbal remedy has ever been prescribed.

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/s/

MANIZHEH SIAHPOUSHAN
10/26/2011

ZACHARY A OLESZCZUK
10/26/2011

CAROL A HOLQUIST
10/26/2011

Department of Health and Human Services

Public Health Service

Food and Drug Administration

Center for Drug Evaluation and Research

Office of Surveillance and Epidemiology

Date:	September 15, 2010
Application Type/Number:	NDA 022200
Through:	Denise P. Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis
From:	Zachary Oleszczuk, PharmD, Team Leader Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name(s):	Bydureon (Exenatide for Extended-release Injectable Suspension) 2 mg per vial
Applicant:	Amylin
OSE RCM #:	2010-1458

1 INTRODUCTION

This re-assessment of the proposed proprietary name, Bydureon, is written in response to the anticipated approval of this NDA within 90 days from the date of this review. DMEPA found the proposed name, Bydureon, acceptable in OSE Reviews #2008-687 and 2009-2193, dated February 2, 2010. DDMAC reviewed the proposed name on May 7, 2008, November 25, 2009, and on July 8, 2010, and had no concerns regarding the proposed name from a promotional perspective. Furthermore, the review Division did not have any concerns with the proposed name, Bydureon, during our initial review.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. We used the same search criteria used in OSE Reviews #2008-687 and 2009-2193, dated February 2, 2010, for the proposed proprietary name, Bydureon. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern.

Additionally, DMEPA searched the United States Adopted Names (USAN) stem list to determine if the name contains any USAN stems as of the last USAN update. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors.

The searches of the databases yielded two new names (Dyclonine and (b) (4) thought to look similar to Bydureon and represent a potential source of drug name confusion. However, our failure mode and effect analysis (FMEA) determined that the name similarity between Bydureon and the two names was unlikely to result in medication errors in the usual practice setting (see Appendix A). Additionally, DMEPA staff did not identify any USAN stems in the proposed proprietary name, Bydureon, as of August 17, 2010.

3 CONCLUSIONS AND RECOMMENDATIONS

The re-review of the proposed proprietary name, Bydureon, did not identify any additional names thought to look or sound similar to the proposed name since our last review. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Bydureon, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Metabolism and Endocrinology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

4 REFERENCES

1. OSE reviews # 2008-687 and 2009-2193, Proprietary Name Review Bydureon, February 2, 2010, Duffy, F.

2. Drugs@FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)

Drugs@FDA contains most of the drug products approved 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, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

3. USAN Stems (http://www.ama-assn.org/ama/pub/category/4782.html)

USAN Stems List contains all the recognized USAN stems.

4. Division of Medication Error Prevention and Analysis Proprietary Name Consultation Request

Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis for review. The list is generated on a weekly basis from the Access database/tracking system.

APPENDICES

Appendix A: Products with no overlap in strength and dose with Bydureon.

Product name with potential for confusion	Similarity to proposed proprietary name	Strength	Usual Dose (if applicable)
Bydureon **(Exenatide extended-release) for injectable suspension**		**2 mg**	**Usual dose: 2 mg subcutaneously once weekly**
(b) (4) *** (Dyclonine) The proprietary name is the (b) (4) The established name has been marketed in the US, however the product was discontinued. The Agency determined that the product was not discontinued or withdrawn for safety or efficacy reasons determination.	Look	Topical Solution: 0.5% and 1%	As with all local anesthetics, the dosage varies and depends up the are to be anesthetized, vasularity of the tissues, individual tolerance and the technique of anesthesia. The lowest dosage needed to provide effective anesthesia should be administered. Usually 4 mL to 30 mL of 1% is sufficient. Apply topically prior to procedure.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22200	ORIG-1	AMYLIN PHARMACEUTICALS INC	Bydureon (exenatide LAR)

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/s/

ZACHARY A OLESZCZUK
09/15/2010

DENISE P TOYER
09/15/2010

Department of Health and Human Services

Public Health Service

Food and Drug Administration

Center for Drug Evaluation and Research

Office of Surveillance and Epidemiology

Date:	February 2, 2010
To:	Mary Parks, MD Director, Division of Metabolic and Endocrinology Products
Through:	Kellie Taylor, PharmD, MPH, Associate Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis
From:	Felicia Duffy, RN, BSN, MSEd, Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name Review
Drug Name:	Bydureon (Exenatide for Extended-release Injectable Suspension) 2 mg per vial
Application Type/Number:	IND 067092 NDA 022200
Applicant:	Amylin
OSE RCM #:	2008-687 and 2009-2193

** Note: This review contains proprietary and confidential information that should not be released to the public. **

CONTENTS

EXECUTIVE SUMMARY

Bydureon is the proposed proprietary name for exenatide for extended-release injectable suspension. Exenatide is currently marketed as an injection by the same Applicant under a different proprietary name (Byetta) for the same indication of use. However, Byetta is not an extended-release injection, and it is administered twice daily unlike this proposed product which is to be administered once weekly. Thus, Bydureon represents a dual proprietary name for this product. This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly. Considering the use of a dual proprietary name and other aspects of the proposed name, our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Our assessment is consistent with the findings of the External Proprietary Name Risk Assessment submitted by the Applicant. Thus, DMEPA finds the proposed proprietary name, Bydureon, acceptable for this product.

If approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Metabolism and Endocrinology Products (DMEP) should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This consult was written in response to a request from Amylin for an assessment of the proposed proprietary name, Bydureon, regarding its potential confusion with other proprietary or established drug names in normal practice settings.

In requesting to use the name Bydureon for this application, the Applicant is requesting to use dual proprietary names to market exenatide since exenatide is currently marketed as Byetta. Exenatide injection is already marketed as Byetta for the same indication for use, but with a different dosage form and frequency of administration.

DMEPA attended a pre-NDA meeting with the Applicant on June 24, 2008. We recommended that the Applicant conduct a Failure Mode and Effects Analysis (FMEA) to evaluate whether a new proprietary name or utilization of an extension of the Byetta name would be less error-prone. The Applicant submitted two separate FMEAs: one conducted by Drug Safety Institute (DSI) dated October 13, 2008, and one conducted by Med-E.R.R.S dated March 21, 2009.

Additionally, container labels, carton and insert labeling, patient package insert labeling, and instruction for use were provided for review and comment and will be reviewed in a separate review (OSE review 2009-2211).

The Applicant also submitted an independent trademark safety evaluation by Medical Error Recognition and Revision Strategies, Inc. (Med-ERRS) which focused on the look-alike and sound-alike risks associated with the proposed name, Bydureon.

1.2 PRODUCT INFORMATION

Bydureon (exenatide extended-release for injectable suspension) is a long-acting formulation of exenatide supplied as a microsphere formulation. It is an incretin mimetic indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. The recommended dose is 2 mg administered

subcutaneously once weekly. Bydureon will be supplied in a single use tray. Each tray will contain one vial of 2 mg exenatide, one prefilled syringe containing (b) (4) mL diluent, one vial connector, and two needles. The entire Bydureon kit should be stored in the refrigerator and protected from light until use. Bydureon should be administered immediately after suspension of the powder into the diluent. It will be supplied in single-use trays, four trays within a carton.

Table 1: Summary of Product Characteristics of Bydureon and Byetta

	Bydureon (NDA 022200)	**Byetta (NDA 021773)**
Indication	Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.	Indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Strength	2 mg per vial	5 mcg pen and 10 mcg pen
Dose	2 mg	5 mcg to 10 mcg
Dosage Form	Powder for injectable suspension	Injection (solution)
Route of Administration	Subcutaneous	Subcutaneous
Frequency of Administration	Once weekly	Twice daily
How Supplied	4 single-dose kits. Each kit contains: -One vial 2 mg exenatide extended-release -One prefilled syringe containing 0.65 mL diluent -One vial connector -Two needles specific to the deliver system	250 mcg/mL exenatide in: 5 mcg per dose, 60 doses, 1.2 mL prefilled pen 10 mcg per dose, 60 doses, 2.4 mL prefilled pen
Storage	Refrigerator	Refrigerator

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1 and 2.2 identify specific information associated with the methodology for the proposed proprietary name, Bydureon.

2.1 SEARCH CRITERIA

The DMEPA staff considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'B' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.[1,2]

[1] Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at http://www.ismp.org/Tools/confuseddrugnames.pdf

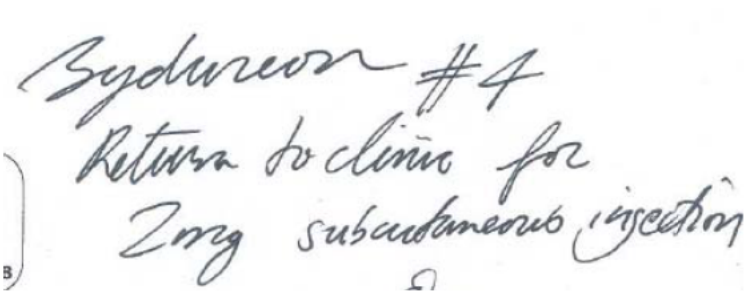
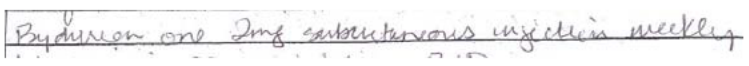
To identify drug names that may look similar to Bydureon, the staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (eight letters), upstrokes (two, capital letter 'B', lower case 'd'), downstrokes (one, lower case 'y'), cross-strokes (none), and dotted letters (none). Additionally, several letters in Bydureon may be vulnerable to ambiguity when scripted, including the letter 'B' may appear as 'K', 'P', 'R', 'Z', lower case 'a', 'e', 'h', 'l', 't', or 'v'; lower case 'y' may appear as a lower case 'g', 'j', 'p', or 'z'; lower case 'd' may appear as 'cl', 'l', or 't'; lower case 'u' may appear as 'a', 'c', 'i', 'o', or 'v'; lower case 'r' may appear as lower case 'n' or 'v'; lower case 'e' may appear as lower case 'a', 'i', or 'o'; lower case 'o' may appear as a', 'e', or 'u'; and lower case 'n' may appear as lower case, 'r', 'u', or 'v'. As such, the staff also considers these alternate appearances when identifying drug names that may look similar to Bydureon.

When searching to identify potential names that may sound similar to Bydureon, the medication error staff search for names with similar number of syllables (four), stresses (BY-du-re-on, by-DU-re-on, by-du-RE-on, and by-du-re-ON), and placement of vowel and consonant sounds. In addition, several letters in Bydureon may be subject to interpretation when spoken, including the letter 'B' which may be interpreted as 'V'; the letter 'd' may be interpreted as 't'; or the letters '-eon' may be interpreted as '-ia', '-ium', or '-iron'. The Applicant's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

2.2 FDA Prescription Analysis Studies

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following inpatient medication orders, outpatient and verbal prescriptions were communicated during the FDA prescription studies.

Figure 1. Bydureon Study (conducted on November 23, 2009)

HANDWRITTEN PRESCRIPITON AND MEDICATION ORDER	VERBAL PRESCRIPTION
Outpatient Prescription:  	Bydureon Dispense #4 Return to clinic every week for 2 mg subcutaneous injection
Inpatient Medication Order :  	

2.3 Adverse Event Reporting System

[2] Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

Since exenatide is currently marketed, the Division of Medication Error Prevention and Analysis reviewed OSE review #2007-1413 (Byetta User Manual Labeling Revisions) which contains postmarketing data extrapolated from the FDA Adverse Events Reporting System (AERS) pertaining to exenatide.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The search yielded a total of 40 names as having some similarity to the name Bydureon.

Twenty-eight of the 40 names were thought to look like Bydureon; these names include: Anteron, Enduron, Roferon, Eryderm, Pylera, Byclomine, Bydramine, Bydaxin, Hycodan, Hylenex, Hydrea, Hyalase, Fuzeon, Lysodren, Blocadren, Ridaura, Zydone, Byetta, Kybernin P, Budesonide, Zemuron, Betaseron, Biperiden, Beheparon Cap, Adheron Liq, Benuron, Bystolic, and Bentyron. Three names were thought to sound like Bydureon; these names include: Iomeron, Bidil, and Bupropion. Nine names (Bydureon, Budeprion/Budeprion SR, (b) (4) ***, (b) (4) ***, (b) (4) ***, Vytorin, Byosan, Pydirone, and Thydron) were thought to look and sound similar to Bydureon.

DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, November 30, 2009.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by the medication error prevention staff (see section 3.1 above), and noted no additional names thought to have orthographic or phonetic similarity to Bydureon.

DDMAC had no concerns regarding the proposed names, Bydureon, from a promotional perspective, and did not offer any additional comments relating to the proposed name.

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 23 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. About 35% of the participants (n=8) interpreted the name correctly as 'Bydureon,' with correct interpretation occurring more frequently in the written studies. The remainder of the responses misinterpreted the drug name. The majority of misinterpretations occurred in the phonetic prescription study, with the beginning of Bydureon reported as 'V' instead of 'B'. Additionally, '-dureon' was phonetically misinterpreted as '-duria', '-buviron', '-durium', and 'turin'. In the written prescription studies, the beginning of Bydureon (By-) was misinterpreted as 'Zy-' by four respondents and, as Ve-' by one respondent. The ending of Bydureon (-dureon) was misinterpreted as '-division' by one respondent, as '-durien' by one respondent, as '-durion' by one respondent, as '-duron' by one respondent, and as
'-derium' by one respondent. See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.4 ADVERSE EVENT REPORTING SYSTEM (AERS)

In OSE review #2007-1413 (Byetta User Manual Labeling Revisions), we reviewed postmarketing data from the FDA Adverse Events Reporting System (AERS) pertaining to exenatide. The majority of medication errors with exenatide involved administration errors of the drug product related to the use of the multi-dose pen device. The pen device errors related to the lack of feedback from the pen device, device malfunction, and knowledge deficit about how to use the device. Since Bydureon is not supplied as a multi-dose pen device, we do not anticipate the same type of medication errors as seen with Byetta.

*** **Note: This is proprietary and confidential information that should not be released to the public.** ***

There were no reports of errors related to name confusion with Byetta or with the established name, exenatide.

3.5 External Proprietary Name Risk Assessments of Bydureon Look-Alike/Sound-Alike Potential

The Applicant submitted an independent risk assessment of the name, Bydureon, conducted by a consulting firm, Medical Error Recognition and Revision Strategies, Inc. (Med-ERRS) dated November 2007. Med-ERRS identified and evaluated one drug name, Budeprion (which includes Budeprion SR and Budeprion XL). This drug was thought to have some potential for look-alike confusion with the name, Bydureon. Budeprion was previously identified in the medication error prevention staff search as having look-alike and sound-alike similarities with Bydureon. Additionally, Med-ERRS evaluated the use of a dual name for this product. Med-ERRS concluded that "despite some safety concerns, the proposed proprietary name, Bydureon, may be an acceptable candidate from a safety standpoint".

3.6 External Failure Mode and Effects Analysis of Naming Convention

The Applicant submitted two studies, one from DSI and one from Med-ERRS. The Failure Mode and Effects Analysis (FMEA) conducted by Drug Safety Institute (dated October 13, 2008), concluded that "a dual proprietary naming strategy carries a slightly higher safety risk relative to potential medication errors compared to marketing under the Byetta plus Modifier naming strategy." Their conclusion is based on the resultant calculation of the Risk Priority Number (described in 3.6.1 below).

The FMEA conducted by Med-ERRS (dated March 2009) concluded that each naming convention carries some risk of confusion and potential error, however using Bydureon as a dual trademark is a better choice from a safety standpoint.

3.6.1 DSI FMEA

The DSI FMEA used two scenarios and customized failure modes for each scenario which reflect unique process categories such as ordering, storing, prescribing, dispensing and/or administration of the existing product 'Byetta' or the proposed product, 'Brand X' or 'Byetta plus Modifier'. The two scenarios evaluated using this methodology were:

1. The co-existence of 'Byetta' and 'Byetta plus Modifier'
2. The co-existence of 'Byetta' and 'Brand X'

The failure modes for each scenario was rated by four pharmacists on the DSI staff using a pre-determined scale of 1 to 10 based three criteria: likelihood, severity, and detectability of each failure mode. Each criterion was given a score by each team member using the operational definitions provided in the chart below:

Value	Likelihood of Occurrence	Severity of Effect	Detectability
1	Remote	None	Immediately detectable
2	Very low	Very minor effect	Found early
3	Low	Minor	Usually found
4	Low to moderate	Low to moderate	Probably found
5	Moderate	Moderate	May be found
6	Moderate to high	Moderate to high	Less than 50% chance of detection
7	High	High	Unlikely to be detected
8	Very High	Very High	Very unlikely to be detected

9	Extremely High	Hazardous	Extremely unlikely to be detected
10	Almost Certain	Disastrous	Almost impossible to detect

The resultant scores from each of the four team members were averaged for each of the three criteria. The averaged scores for likelihood, severity, and detectability were then multiplied to determine the Risk Priority Number (RPN) which takes into account how risky a failure mode is and also the ability to detect the associated risk. The higher the RPN the greater the risk for failure with the process.

The Byetta plus Modifier scenario evaluated 11 failure modes. The RPN for Byetta plus Modifier ranged from 20 to 60, with an average value of 40. The top three failure mode error types for this naming convention were: wrong drug, wrong dose, or a combination of the two. The RPN value for the top three failure modes was 60, 52, and 51 with an average score of 54.

The dual proprietary name strategy scenario evaluated seven failure modes. The RPN for the use of a dual proprietary name ranged from 18 to 119 with an average value of 60. The top three failure mode for the dual proprietary name strategy was the same type of error for each failure mode: wrong dose. The RPN value for the top three failure modes was 199, 76, and 76 with an average score of 90.

The DSI FMEA demonstrated that "both the modifier strategy and the dual proprietary name strategy show a low-to-moderate risk strategy for the proprietary name of the 2 mg once weekly injection." However, it is important to note that the overall scale used in evaluating the RPN values is 1 to 1000 [which] suggests either strategy is low in risk."

The DSI FMEA also identified what practitioner is in the best position to prevent the medication error from occurring and what could be done to prevent the medication error from occurring.

3.6.2 Med-ERRS FMEA

The Med-ERRS FMEA used a group of 12 internal practitioners to develop "worst case" scenarios for the product 'Byetta plus Modifier' or the proposed proprietary name product 'Bydureon'. The panel assessed the potential failure modes throughout the drug use process such as procurement, prescribing, dispensing, and administration of the product 'Byetta plus Modifier' or the proposed proprietary named product 'Bydureon'.

The scenarios were depicted in a flow-chart diagrams. Med-ERRS also used tables to describe the pros and cons of using a modifier with Byetta and using the dual proprietary name, Bydureon (see Appendix P).

Med-ERRS described the worst case scenario with the use of "Byetta plus a modifier" which results in the original Byetta product being dispensed and the patient using it weekly instead of twice daily. MedERRS identified the greatest risk associated with the use of using "Bydureon" is that he patient could get the active ingredient under both medication names, resulting in concomitant administration of both exenatide formulations. Med-ERRS did not indicate which of these scenarios would occur more frequently.

We note Med-ERRS mentioned that careful consideration should be given with the use of dual trade names related to the unique potential for medication errors associated with unfamiliarity of a new formulation. Med-ERRS also indicated that an alternative to a dual trade name for the proposed product is to use a modifier such as "weekly", which has been used to designate a once weekly dosage formulation (e.g., Prozac Weekly).

4 DISCUSSION

The proposed Bydureon (exenatide extended-release) for injecatable suspension product will be an extension of the exenatide product line manufactured by the Applicant and marketed under the proprietary name Byetta. Although both products contain the same active ingredients, Bydureon is an extended-release formulation. The differences between Bydureon and Byetta are the doses (2 mg vs. 5 mcg and 10 mcg), frequency of administration (once weekly vs. twice daily), and dosage form (powder for injectable suspension vs. solution for injection). Bydureon will be available as a kit where it must be reconstituted prior to administration, whereas

Byetta is a prefilled mulitdose pen injector. See chart on page 4 for a comparison of Bydureon and Byetta characteristics.

The Applicant proposes a new and different proprietary name for this product. In evaluating this proprietary name, we considered whether the product could be safely managed using the name, Bydureon, and considered the risk of inadvertent concomitant administration of the exenatide products.

4.1 EXENATIDE PRODUCT LINE EXTENSION

The Applicant proposes to market the new exenatide extended-release product under a new proprietary name in order to reduce the risk of confusion between Bydureon and Byetta. The Applicant indicated that they believe there are benefits to using a dual proprietary name (Bydureon) to distinguish between the two formulations of exenatide. In the Applicant's March 28, 2008 cover letter, the Applicant indicates:

> *If the exenatide once weekly formulation was identified by a trademark that is close to Byetta (such as with the addition of a suffix), there is a possibility that the patient could receive an inadvertent underdose (i.e., the Byetta formulation once weekly) or overdose (i.e., the long-acting exenatide once weekly formulation twice daily).*

As with any product line extension, the naming convention must be considered whether it is an extension of an existing name or the introduction of a new name, in order to minimize medication errors. Based on postmarketing experience with other product line extensions where Applicants have used the same proprietary name plus a modifier, we believe that the naming convention of adding a modifier to the existing name Byetta could lead to errors [3]. For example, the potential exists for prescribers to omit the modifier when prescribing the product or to overlook the modifier mistakenly select the wrong product on electronic computer menus when prescribing medicines electronically. Additionally, similar computer selection errors may occur in the pharmacy when dispensing the product if the modifier is overlooked even though the doses and strengths of the exenatide and extended-release exenatide differ (5 mcg and 10 mcg vs. 2 mg). Lastly, selection errors may occur if they are stored side-by-side within pharmacy refrigerators, but the potential for such errors may be mitigated through well-differentiated carton labels and this risk will be considered further in our forthcoming labeling review. With any of the errors involving confusion between exenatide and extended-release potential exists for patients to be underdosed (immediate release product dosed once weekly) or overdosed (extended-release formulation twice daily).

There are also risks associated with using dual proprietary names. With the use of a new proprietary name, Bydureon, there is a risk of concomitant therapy of exenatide if practitioners and patients fail to recognize that both Bydureon and Byetta contain exenatide.

The Applicant submitted two independent FMEA analyses assessing the risks associated with the various nomenclature approaches. One limitation of the DSI FMEA is the limited number of participants in the FMEA (four participants) and the make-up of the team. The analysis conducted by DSI presented data that indicates that the use of a dual proprietary name for this application carries a slightly higher risk for medication errors compared to using the current name (Byetta) plus a modifier. However, DSI considers both naming strategies safe since the average and range of the RPN for each strategy was not substantially different (see 3.6.1). Additionally, DSI identified a greater number of failures with the Byetta plus modifier scenario indicating that this strategy is more vulnerable to error (11 failure modes versus 7 failure modes), even though the average RPN was not substantially different from the alternate trade name scenario.

Similarly, the analysis by Med-ERRS also concluded that each naming convention carries some risk of confusion and error. However, unlike DSI, Med-ERRS concluded that Bydureon as a dual proprietary name is a safer option based on the results of their FMEA. Med-ERRS rationale is that if Bydureon is prescribed with ambiguous directions (such as "as directed"); the patient is likely to receive the correct medication with the

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

correct dosing instructions for administration, with the least chance that the prescription would have to be clarified with the prescriber. According to Med-ERRS, if an error did occur resulting in the use of Byetta and Bydureon concurrently, they anticipate that the harm to the patient would be less severe than the harm that may result from an underdose of exenatide if Byetta were to be administered once weekly (which they indicated as their "worse case" scenario if the name was "Byetta plus a modifier", and the modifier was omitted or overlooked causing Byetta to be dispensed for once weekly administration). Med-ERRS noted that that errors were more likely to occur if this product were managed using "Byetta plus a modifier" given the greater number of failure modes identified with this strategy and that such errors may carry a greater likelihood of harm. One limitation to their analysis is that they did not consider the risk if Bydureon is administered twice daily, and it is unclear if their conclusion would have been different had they considered this risk.

DMEPA concurs with both analyses with respect to the fact that there are risks involved when extending a product line. We also acknowledge that there are risks associated with using an existing name with a modifier or a dual proprietary name, but that the number of risks may be greater if this product were managed using the name Byetta plus a modifier given the results of the FMEAs submitted. In our analysis of the proposed name Bydureon, we note that the use of the same prefix 'By-' in both proprietary names **By**dureon and **By**etta may help increase practitioner awareness that both products contain the same active ingredient. Thus, we agree with the Applicant that this product may be managed by using a new proprietary name. However, we remain concerned for the potential for concomitant therapy since postmarketing experience with other drug products has shown concomitant therapy to be a common type of error when an active ingredient is marketed under two or more names. [4] Also, errors still may occur when prescribers order either product using the established name. Nevertheless, because we anticipate that medication errors will occur regardless of the proprietary name used, DMEPA plans to monitor for such errors after approval of Bydureon.

4.2 BYDUREON ASSESSMENT OF RISK OUTSIDE OF THE EXENATIDE PRODUCT LINE

In evaluating the proposed name outside of the product line, we considered the name from a promotional and safety perspective. DDMAC did not have concerns with the proposed name from a promotional perspective. DMEP and DMEPA concurred with these findings. DMEPA considered the use of a dual name (see section 4.1) and other aspects of the name that might render the name unacceptable.

DMEPA identified and evaluated 40 names for their potential similarity to the proposed name. Twenty-three of the 40 names lacked orthographic and/or phonetic similarity and were not evaluated further (see Appendix C). Failure mode and effect analysis (FMEA) was then applied to determine if the potential name could potentially be confused with the remaining 17 names and lead to medication errors. This analysis determined that the name similarity between Bydureon was unlikely to result in medication errors with any of the 17 names for the reasons presented in Appendices D through N. On December 14, 2009, DMEPA notified the Division of Metabolism and Endocrinology Products via e-mail that we had no objections to the proposed proprietary name Bydureon. Per e-mail correspondence from DMEP on December 30, 2009, they indicated that they concur with our assessment of the proposed proprietary name, Bydureon.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name is not promotional. However, the safety review of the name indicates that use of a dual name for this product carries some risk of confusion and error as does having the root name "Byetta plus a modifier". We have concluded that Bydureon is acceptable because the use of the same prefix 'By-' in both proprietary names **By**dureon and **By**etta may help increase practitioner awareness that both products contain the same active ingredient, there is less risk for modifier omission, and the dual name may help to increase awareness that Bydureon and Byetta are administered differently (different frequency of administration).

[4] The Institute for Safe Medication Practices. "Revatio=Sildenafil=Viagra". January 2009

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. If the approval of this supplement is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

5.1 COMMENTS TO THE DIVISION

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Margarita Tossa, OSE Project Manager, at 301-796-4053.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Metabolism and Endocrinology Products (DMEP) should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

5.2 COMMENTS TO THE APPLICANT

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

If approval of the NDA is delayed beyond 90 days from the date of this review, the proprietary name must be re-reviewed prior to the new approval date.

If **any** of the proposed product characteristics are altered prior to approval of this NDA, the proprietary name should be resubmitted for review.

6 REFERENCES

1. Adverse Events Reporting System (AERS)

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufactures that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential postmarketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

2. Micromedex Integrated Index (http://csi.micromedex.com)

Contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

3. Phonetic and Orthographic Computer Analysis (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion. This is a database which was created for DMEDP, FDA.

4. Drug Facts and Comparisons, online version, St. Louis, MO (http://factsandcomparisons.com)

Drug Facts and Comparisons is a compendium organized by therapeutic Course; contains monographs on prescription and OTC drugs, with charts comparing similar products.

5. AMF Decision Support System [DSS]

DSS is a government database used to track individual submissions and assignments in review divisions.

6. Division of Medication Error Prevention and Analysis proprietary name consultation requests

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

7. Drugs@FDA (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm)

Drugs@FDA contains most of the drug products approved 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 and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologicals, discontinued drugs and "Chemical Type 6" approvals.

8. Electronic online version of the FDA Orange Book (http://www.fda.gov/cder/ob/default.htm)

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

9. USPTO (http://www.uspto.gov)

Provides information regarding patent and trademarks.

10. Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

11. Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at (www.thomson-thomson.com)

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and tradenames that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

12. Natural Medicines Comprehensive Databases (www.naturaldatabase.com)

Contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

13. Stat!Ref (www.statref.com)

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

14. USAN Stems (http://www.ama-assn.org/ama/pub/category/4782.html)

List contains all the recognized USAN stems.

15. Red Book Pharmacy's Fundamental Reference

Contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

16. Lexi-Comp (www.lexi.com)

A web-based searchable version of the Drug Information Handbook.

17. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

18. FDA Documenting Archiving, Reporting & Regulatory Tracking System [DARRTS]

DARRTS is a government database used to organize Applicant and Sponsor submissions as well as to store and organize assignments, reviews, and communications from the review divisions.

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. 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]

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [6] DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.[7] DMEPA provides the product characteristics considered for this review in section one.

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

[6] Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

[7] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly in spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name.

Type of similarity	**Considerations when searching the databases**		
	Potential causes of drug name similarity	*Attributes examined to identify similar drug names*	*Potential Effects*
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	• Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication • Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the DMEPA staff to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA Prescription Analysis Studies

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 the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. 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 send their interpretations of the orders via e-mail to DMEPA.

4. Comments from the OND Review Division

DMEPA requests the Office of New Drugs (OND) responsible for the application for its comments or concerns with the proposed proprietary name and 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 DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the Safety Evaluator's assessment.

The OND is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys its decision to accept or reject the name. OND is requested to concur/not concur with DMEPA's final decision.

5. External Proprietary Name Risk Assessment

DMEPA conducts an independent analysis and evaluation of the data provided, and responds to the overall findings of the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's risk assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in usual practice settings.

After the safety evaluator has determined the overall risk assessment of the proposed name, the Safety Evaluator compares the findings of the overall risk assessment to the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the DMEPA staff's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the DMEPA staff provides a detailed explanation of these differences.

6. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.[8] When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

[8] Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

"Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?"

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

"Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?"

The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
2. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
5. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error and, thereby, would render the proposed name acceptable.

In the event that DMEPA objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEPA will provide a

contingency objection based on the date of approval. Whichever product, the Agency approves first has the right to use the proprietary name, while DMEPA will recommend that the second product to reach approval seek an alternative name.

The threshold set for objection to the proposed proprietary name may seem low to the Sponsor. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Sponsor can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

Appendix B: CDER Prescription Study Responses

Outpatient Prescription	Voice Prescription	Inpatient Prescription
Bydureon	Byduria	Bydivion
Bydureon	Vibuviron	Bydureon
Bydureon	Vidurium	Bydurien
Bydureon	Vidurium	Bydurion
Bydureon	Vyturin	Byduron
Bydureon		Byduron
Bydureon		Vederium
Zydureon		
Zydureon		
Zydureon		
Zydureon		

Appendix C: Names lacking convincing look-alike and/or sound alike similarities with Bydureon

Proprietary Name	Proprietary Name	Proprietary Name	Proprietary Name	Proprietary Name
Roferon	Budesonide	Bentyron	Ridaura	Benuron
Pylera	Anteron	Iomeron	Zydone	BiDil
Hycodan	Hylenex	Byosan	Byetta	Hyalase
Blocadren	Zemuron	Thydron	Beheparon	
Hydrea	Biperiden	Fuzeon	Adheron	

Appendix D: Proprietary names trademarked in foreign countries

Proprietary Name	Similarity to Bydureon	Country
Bydaxin	Look	Japan

Appendix E: Withdrawn products with no generics available according to the old DSS system. DSS database was replaced with DARRTS database. Name was not transferred into DARRTS and not found in any other databases utilized in proprietary name review

Proprietary Name	Similarity to Bydureon	Status	Source
Pydirone	Look	Withdrawn by Commissioner, Jun 1977	Decision Support System (DSS)

Appendix F: Proprietary name withdrawn, product was never marketed

Proprietary Name	Similarity to Bydureon	Status	Source
(b) (4) ***	Look/Sound	Withdrawn in (b) (4)	DARRTS

Appendix G: Orphan drug designee not approved by the Agency

Proprietary Name	Similarity to Bydureon	Source
Kybernin P	Look	Orphan drugs

Appendix H: Trademarked name by the Applicant

Proprietary Name	Similarity to Bydureon	Source
(b) (4) ***	Look/Sound	(b) (4)

Appendix I: Pending trademarked name by the Applicant in foreign countries

Proprietary Name	Similarity to Bydureon	Source	Country
Bydureon	Look/Sound	Saegis	(b) (4)

*** **Note: This is proprietary and confidential information that should not be released to the public.** ***

Appendix J: A different Applicant initially submitted the name below, but before DMEPA could review the name, the Applicant elected to use another proprietary name for their application, and the name was found acceptable by DMEPA.

Proprietary Name	Similarity to Bydureon	Applicant
(b) (4) *	Look/Sound	(b) (4)

Appendix K: Products with no overlap in strength and dose with Bydureon.

Product name with potential for confusion	Similarity to proposed proprietary name	Strength	Usual Dose (if applicable)
Bydureon **(Exenatide extended-release) for injectable suspension**		**2 mg**	**Usual dose: 2 mg subcutaneously once weekly**
Bydramine (Diphenhydramine HCl) oral solution	Look	12.5 mg/5 mL	12.5 mg to 25 mg po Q4-6 hrs
Bupropion (Bupropion) tablets Bupropion (Bupropion) extended-release tablets	Sound	Tablets: 75 mg, 100 mg Extended-release: 150 mg, 300 mg	Immediate release: usual dose is 300 mg po per day, given 3 times daily. Begin at 200 mg/day, given as 100 mg twice daily. Extended-release: usual dose is 300 mg po per day, given once daily. Begin at 150 mg/day, given as a singe daily dose
Budeprion SR (Bupropion) extended-release tablets Budeprion XL (Bupropion) extended-release tablets	Look/Sound	100 mg, 150 mg 300 mg	Usual dose is 300 mg po per day, given once daily. Begin at 150 mg/day, given as a singe daily dose
Vytorin (Ezetimibe/Simvastatin) tablets	Look/Sound	10 mg/10 mg, 10 mg/20 mg, 10 mg/40 mg, 10 mg 80 mg	10 mg/10 mg to 10 mg/80 mg po daily

Appendix L: Products with a numerical overlap or similar numerical overlap in strength, but with different product characteristics

Product name with potential for confusion	Similarity to Bydureon	Strength/Usual Dose	Differentiating product characteristics
Bydureon **(Exenatide extended-release) for injectable suspension**		**2 mg** **Usual dose: 2 mg subcutaneously once weekly**	
Enduron (Methyclothiazide) tablets	Look	2.5 mg, 5 mg Dose: 2.5 mg-10 mg po once daily	**Dosage form:** Tablets vs. for injectable suspension **Route of administration:** Oral vs. subcutaneous **Indication:** Hypertension vs. diabetes mellitus **Frequency of administration:** Once daily vs. once weekly
Bystolic (Nebivolol) tablets	Look	2.5 mg, 5 mg, 10 mg, 20 mg Dose: 5 mg po once daily	**Dosage form:** Tablets vs. for injectable suspension **Route of administration:** Oral vs. subcutaneous **Indication:** Hypertension vs. diabetes mellitus **Frequency of administration:** Once daily vs. once weekly

Appendix M: Drug names with single strength availability but with differentiating product characteristics

Product name with potential for confusion	Similarity to Product Name	Strength	Usual Dose	Other Differentiating Product Characteristics
Bydureon **(exenatide) for injectable suspension**		**2 mg**	**2 mg subcutaneously once weekly**	
Eryderm (Erythromycin) topical solution	Look	2%	Apply to affected area(s) each morning and evening after skin is washed with warm soap and water and pat dry	**Dosage form:** Topical solution vs. for injectable suspension **Route of administration:** Topical vs. subcutaneous **Indication:** Acne vs. diabetes mellitus **Frequency of administration:** Twice daily vs. once weekly
Byclomine (Dicyclomine HCl) tablets	Look	20 mg	160 mg po per day (in 4 equally divided doses)	**Dosage form:** Tablet vs. for injectable suspension **Route of administration:** Oral vs. subcutaneous **Indication:** Functional bowel/irritable bowel syndrome vs. diabetes mellitus **Frequency of administration:** Four times daily vs. once weekly

Appendix N: Potential confusing name with numerical overlap in strength or dose with Bydureon

Failure Mode: **Name confusion**	**Causes (could be multiple)**	**Effects**
Bydureon **(Exenatide for injectable suspension) extended-release** **2 mg/vial**		**Usual dose:** **2 mg subcutaneously once weekly**
Lysodren (Mitotane) 500 mg tablets **2**g to 10g po per day in divided doses, either 3 or 4 times a day	Orthographic similarity: ('ly-' and 'by-' may appear similar when scripted in lower case letters; both contain 8 letters; both contain an upstroke 'd'; the endings '-ren' and '-reon' may appear similar when scripted) Numerical overlap in dose (**2** grams vs. **2** mg)	Product differences in conjunction with orthographic differences in the names minimize the likelihood of medication error in the usual practice setting. *Rationale:* Lysodren is an oncology drug indicated in the treatment of inoperable adrenal cortical carcinoma. Although Lysodren and Bydureon share a similar numerical dose, Lysodren is dosed in grams whereas Bydureon is dosed in milligrams. Additionally, Lysodren is an oral tablet administered 3 or 4 times a day, and Bydureon is a subcutaneous injection administered once weekly. Orthographically, although Lysodren and Bydureon contain an upstroke 'd', they appear in different positions of the each name (5th position vs. 3rd position). Additionally, the letters '-so-' in the middle of Lysodren may also help to differentiate the names. Despite some overlapping product characteristics, the unit of measure, dosage form, route of administration and frequency of administration minimizes the risk of confusion between Lysodren and Bydureon.
Betaseron (Interferon Beta-1b) 0.3 mg powder for injection	Orthographic similarity: Both begin with 'B'; both contain upstroke letters 't' and 'd' in the third position; 'a' and 'u' may appear similar when scripted; '-er-' and '-re-' are transposed; both end with '-on' Both available as a single strength (0.3 mg vs. 2 mg); Numerical dosage and volume similarity (2 mg vs. 0.25 mg) and 0.75 mL (b) (4) dosage form	Orthographic differences in the names minimize the likelihood of medication error in the usual practice setting. *Rationale:* Betaseron does not contain any downstroke letters, whereas Bydureon contains a downstroke 'y' in the second position. Although both names contain an upstroke letter ('t' vs. 'd'), the cross stroke 't' may provide some differentiation between the names. Betaseron is indicated for the treatment of multiple sclerosis. It is dosed on the following titration schedule: Wk 1-2: 0.0625 mg (0.25 mL) Wk 3-4: 0.125 mg (0.5 mL) Wk 5-6: 0.187 mg (0.75 mL)

	(lyophilized powder); route of administration (subcutaneous); storage conditions (refrigerator vs. refrigerate after reconstitution) Both supplied are supplied in kits	Wk 7+: 0.25 mg (1 mL) Despite the fact that both products are available as a single strength, the Betaseron dose must be specified because it will vary based upon the titration schedule. The Bydureon dose is fixed at 2 mg, and does not vary. Although there is a numerical overlap with Betaseron 0.**2**5 mg and Bydureon **2** mg, the likelihood of misinterpreting 0.25 mg as 2 mg is minimal because one would have to omit the leading zero and overlook the number '5'. Additionally, both products may (b) (4) mL). However, it is unlikely that Bydureon will be prescribed by volume because it is drug that has a fixed strength and dose of 2 mg. Therefore, Bydureon will mostly likely be prescribed by its milligram strength, or the strength may be omitted completely for Bydureon. In either case, this differentiating factor will help to minimize confusion between Betaseron and Bydureon. Furthermore, both differ in frequency of administration (every other day vs. once weekly), which provides an additional differentiation between the drug products. Despite some similarities and overlapping product characteristics, the product strength, and dosing instructions minimizes the risk of confusion between Betaseron and Bydureon.

Appendix O: DSI FMEA summary

SCENARIO 1: THE CO-EXISTENCE OF BYETTA AND BYETTA PLUS MODIFIER

There were 11 failure modes identified for BYETTA co-existing in the market place with BYETTA plus MODIFIER. The results for each failure mode are then displayed which shows the data collected from the respondents (referred to as A, B, C, and D). The following table displays the failure modes that were created and analyzed in the FMEA for Scenario #1

SCENARIO #1

1	A physician intends for the patient to get the new Byetta once a week product. He writes the order for Byetta – Use Weekly. Patient receives BYETTA 5 mcg (intended for twice daily administration) with the directions "use once weekly as directed" Patient injects 5 mcg once a week for a total of 4 weeks.
2	Order is placed for BYETTA plus MODIFIER 2 mg and BYETTA 5 mcg is selected from the drop down computerized pick list leading to a dispensing error. Patient receives and injects 5 mcg once a week and continues to take for 2 months.
3	Patient been given a prescription to switch from BYETTA 10mcg BID to BYETTA plus MODIFIER 2 mg. The patient thought that 2 mg was the same as 20 and decided to save money and administer two-10 injections once a week.
4	Order is placed for BYETTA 10 and BYETTA plus MODIFIER is selected from the inventory-storage refrigerator leading to a dispensing error. Patient who received the wrong drug was also taking warfarin 2mg QAM.
5	Order is placed for BYETTA plus MODIFIER and BYETTA 5 is selected from the inventory-storage refrigerator leading to a dispensing error
6	Order is placed with the distributor for a new prescription for BYETTA plus MODIFIER. The order was placed for BYETTA when selected from an inventory catalog. The prescription label for BYETTA plus MODIFIER was affixed to the product that came into the order the next day.
7	Patient is told by his physician to increase the amount of BYETTA from 5mcg to 10mcg. Patient has used BYETTA 5mcg and also has BYETTA plus MODFIER at home. Rather than get a new prescription, patient decides to reconstitute the BYETTA plus MODIFIER an injects ½ the vial amount in the morning before breakfast and the other ½ in the evening before dinner. (Please consider the information that once opened, BYETTA plus MODIFIER (may solidify)
8	Physician writes prescription for "exenatide use as directed weekly". Pharmacist checks patient profile and dispenses the same prescription as the last prescription – BYETTA 10. The physician meant for the patient to have the 'NEW – BYETTA plus MODIFIER" product. Patient was very happy he did not have to 'mix anything' when he got home and injected the 10mcg once a week.
9	Pharmacy clerk orders BYETTA 10mcg instead of the needed BYETTA plus MODIFIER due to the names in the computer order entry being in alphabetical order; Prescription label was generated according to the prescription which was inject once weekly; The label was placed on the wrong product when it arrived. Patient received "once weekly' injection instruction on the 10mcg BYETTA box.
10	Physician sees a new patient and asks for all their medication history; Patient writes down 'BYETTA injection' and gives it to the physician. The physician does not ask whether or not the patient is prescribing twice daily or once a week; The physician dispenses BYETTA 10mcg and tells the patient to inject twice daily. The patient gets home and 'uses up the other medication' according to the physician's new instruction. Patient had BYETTA plus MODIFIER and INJECTS twice daily for 5 days.
11	Patient receives a new prescription for BYETTA plus MODIFIER from the physician and takes it to the pharmacy. Patient receives 1 month supply of the 2mg SQ weekly exenatide injection. Patient continues to take BYETTA 10mcg twice daily for the month.

SCENARIO #2: THE CO-EXISTENCE OF BYETTA AND BRAND X

Each situation explores possible medication errors that can occur if the manufacturer changes the original brand name, BYETTA and a new product with the same active ingredient, BRAND X is launched into the market place.

The results for each failure mode are then displayed which shows the data collected from the respondents (referred to as A, B, C, and D).

The following table displays the failure modes created and analyzed in the FMEA for Scenario #2.

SCENARIO #2

1	A patient has been injecting BYETTA 10mcg twice daily for a number of years and the physician decides to change the prescription to BRAND X. Not realizing that the new prescription was to replace the old, the patient correctly receives a new prescription for BRAND X; however continued on the Byetta while taking the BRAND X prescription.
2	Patient is told by his physician to increase the amount of BYETTA from 5mcg to 10mcg. Patient has used BYETTA 5mcg and also has BRAND X at home. Rather than get a new prescription, patient decides to reconstitute the BRAND X and injects ½ the vial amount in the morning before breakfast and the other ½ in the evening before dinner. (Please consider the information that once opened, BRAND X may solidify)
3	Patient was diagnosed 5 years ago with Type 2 diabetes; A new physician prescribes BRAND X. Patient is told that the active ingredient is the same as BYETTA – just a higher dose. To use up about 6 weeks of BYETTA pens at home, the patient decides to inject 5 mcg once a week; the mistake is caught after 2 weeks.
4	A patient, who speaks Spanish, is seen by a new physician because his physician is on vacation. The patient has been on BYETTA 5mcg SQ twice daily for Type 2 Diabetes. The new physician selects BRAND X and doesn't realize that the patient has been on BYETTA. He provides a prescription for BRAND X and the patient takes both BRAND X and BYETTA. The patient takes both products for 3 months.
5	A patient has been taking BRAND X for 6 months and goes to see another physician who reads 'exenatide' in the patients chart. The new physician writes a prescription for BYETTA twice daily injections and the patient goes to the pharmacy and gets a new prescription for BYETTA and continues to take BRAND X.. After 1 week the patient begins to have nausea, diarrhea and a feeling of jitteriness and calls his physician.
6	Physician sees a new patient and asks for all their medication history; Patient writes down exenatide and gives it to the physician. The physician does not ask whether or not the patient is taking twice daily or once a week injections; The physician dispenses BYETTA 10mcg and tells the patient to inject twice daily. The patient gets home and 'uses up the other medication' according to the physician's new instruction. Patient had some BRAND X and INJECTS twice daily for 5 days.
7	A physician in an assisted living facility provides a verbal order for a patient for exenatide twice daily. Nurse transcribes the verbal order into physician order as BRAND X twice a day. Patient receives BRAND X and continues for 1 month until the next medication profile review. Hospital orders do not include 'discontinue BYETTA.' For the remaining 30 days patient receives both products.

Table 1 - The top 3 failure modes in Scenario 1 based on highest calculated RPN value.

Scenario	FM#	Process Category	Cause of Error	Type of Error	Consequence to consider for severity	RPN
1	10	Monitoring	Incomplete information gather from medical history	Wrong drug/ Wrong dose	Higher than prescribed dose; 2 mg BID for 5 days	60
1	2	Dispensing Error	Modifier Drop; Computer Mispick	Wrong Drug	Lower Dose than prescribed for 2 months; under dosed - 5 mcg QW	52
1	4	Dispensing Error	Mispick from Pharmacy Shelf in Refrigerator	Wrong Drug	Higher dosage than prescribed in patient taking warfarin	51

Table 2 - The top 3 failure modes in Scenario 2 based on highest calculated RPN value.

Scenario	FM#	Process Category	Cause of Error	Type of Error	Consequence to consider for severity	RPN
2	4	Prescribing Error	Incomplete profile history taken from patient	Wrong dose	higher dose than prescribed for 3 months; overdose of 2 mg QW and 5 mcg BID daily	119
2	5	Prescribing Error	Incomplete profile history taken for patient by physician	Wrong Dose	higher than prescribed for 1 week; overdose of 2 mg QW and 5/10 mcg BID daily for 1 week	76
2	1	Administration Error	Confusion by patient due to distinct brand names	Wrong dose	Higher dose than prescribed; overdose of 2 mg QW and 10 mcg BID daily;	76

Appendix P: Med-ERRS FMEA summary

Figures 1, 2 and 3 illustrate several key scenarios involved in the prescribing dispensing, and administration steps of a prescription using Byetta plus a modifier. Figures 1 and 2 illustrate the three main scrnatiors that initiate from the point of the prescriber. So as to not crowd the information shown in Figure 1, Figure 2 is a 'break out' of the scenarios involved if a modifier is not included in the prescription communication. Figure 3 focuses on administration issues that primarily involve the patient.

Table 4 describes the pros and cons of using a modifier with Byetta.

Figure 4 illustrates several key scenarios involved in the prescribing, dispensing, and administration steps of a prescription using Bydureon.

Table 4 describes the pros and cons of using Bydureon.

Figure 1

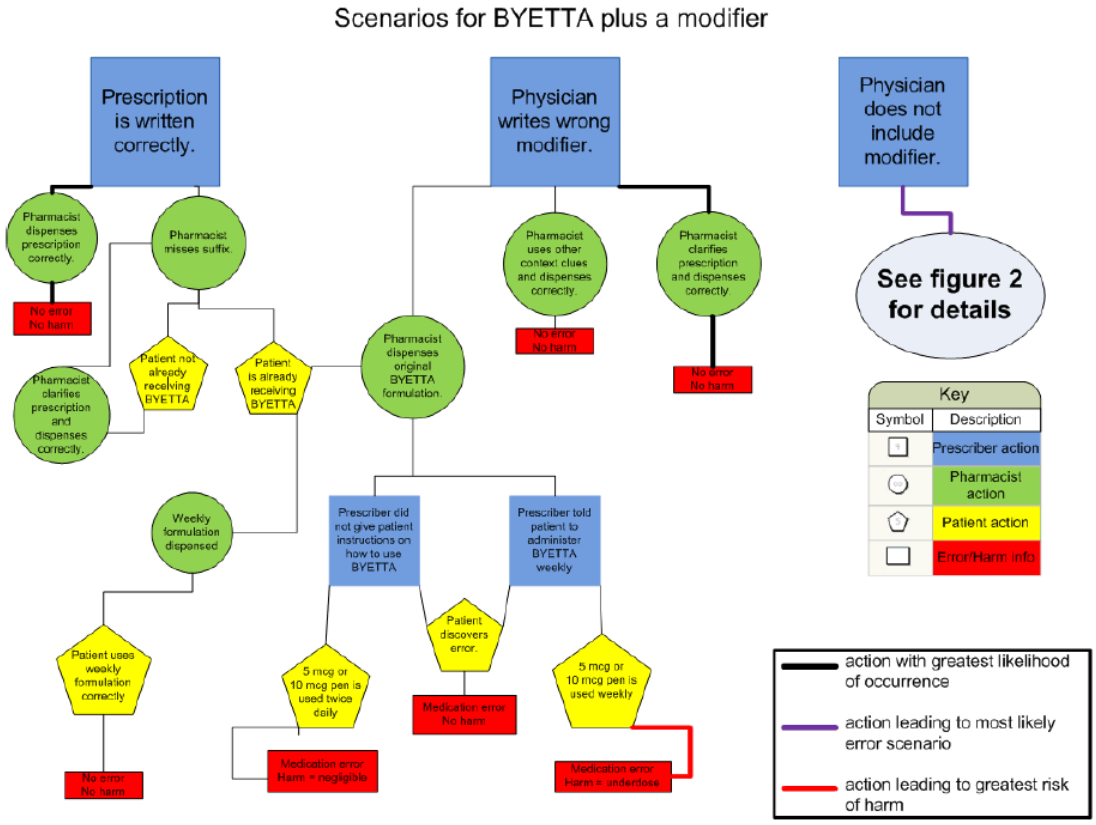


Figure 2

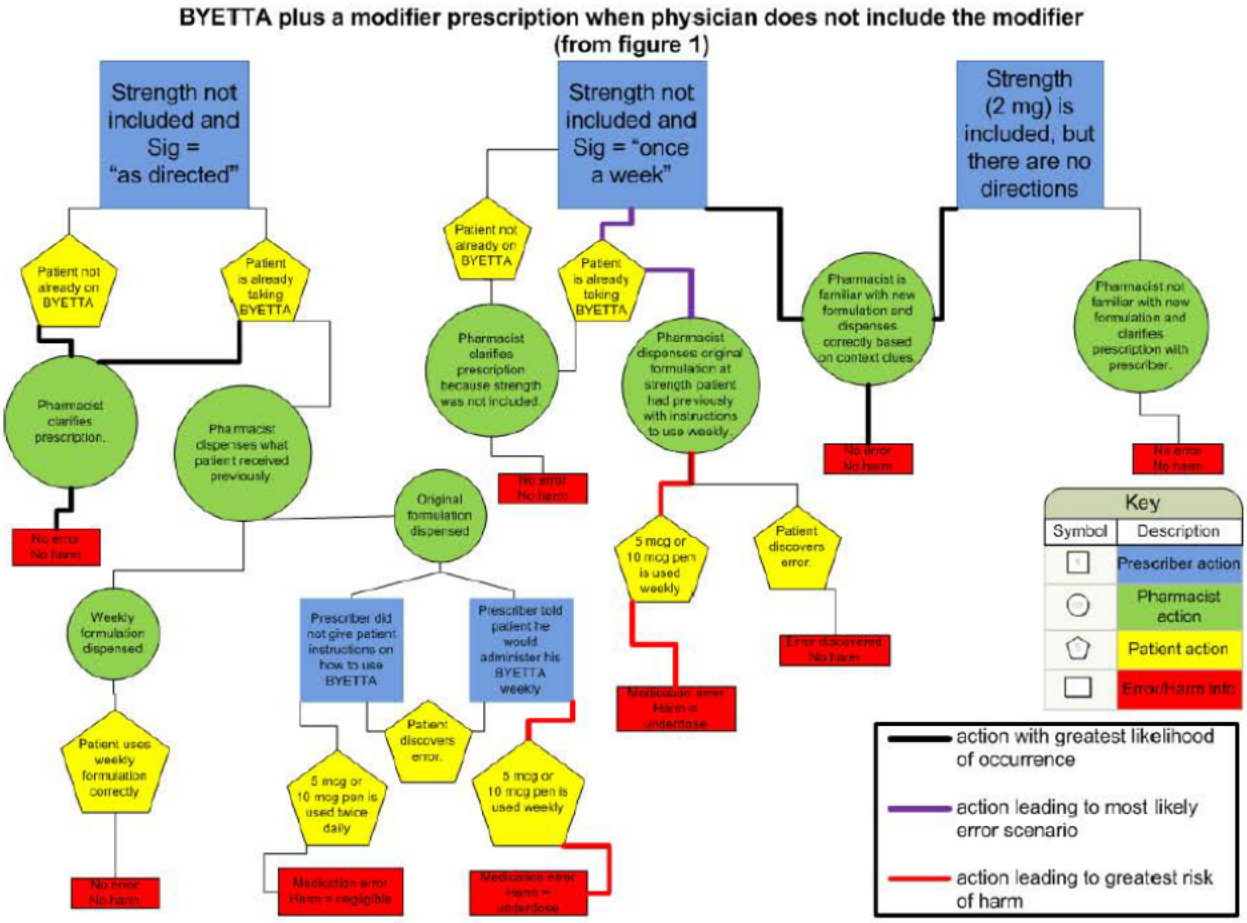

BYETTA plus a modifier prescription when physician does not include the modifier (from figure 1)
Strength not included and Sig = "as directed"
Strength not included and Sig = "once a week"
Strength (2 mg) is included, but there are no directions
Patient not already on BYETTA
Patient is already taking BYETTA
Pharmacist clarifies prescription.
Pharmacist dispenses what patient received previously.
No error No harm
Original formulation dispensed
Weekly formulation dispensed
Patient uses weekly formulation correctly
No error No harm
Prescriber did not give patient instructions on how to use BYETTA
Prescriber told patient he would administer his BYETTA weekly
Patient discovers error.
5 mcg or 10 mcg pen is used twice daily
Medication error Harm = negligible
5 mcg or 10 mcg pen is used weekly
Medication error Harm = underdose
Patient not already on BYETTA
Pharmacist clarifies prescription because strength was not included.
No error No harm
Patient is already taking BYETTA
Pharmacist dispenses original formulation at strength patient had previously with instructions to use weekly.
5 mcg or 10 mcg pen is used weekly
Medication error Harm = underdose
Patient discovers error.
Error discovered No harm
Pharmacist is familiar with new formulation and dispenses correctly based on context clues.
No error No harm
Pharmacist not familiar with new formulation and clarifies prescription with prescriber.
No error No harm
Key
Symbol
Description
Prescriber action
Pharmacist action
Patient action
Error/Harm info
action with greatest likelihood of occurrence
action leading to most likely error scenario
action leading to greatest risk of harm

Figure 3

Administration issues with BYETTA plus a modifier

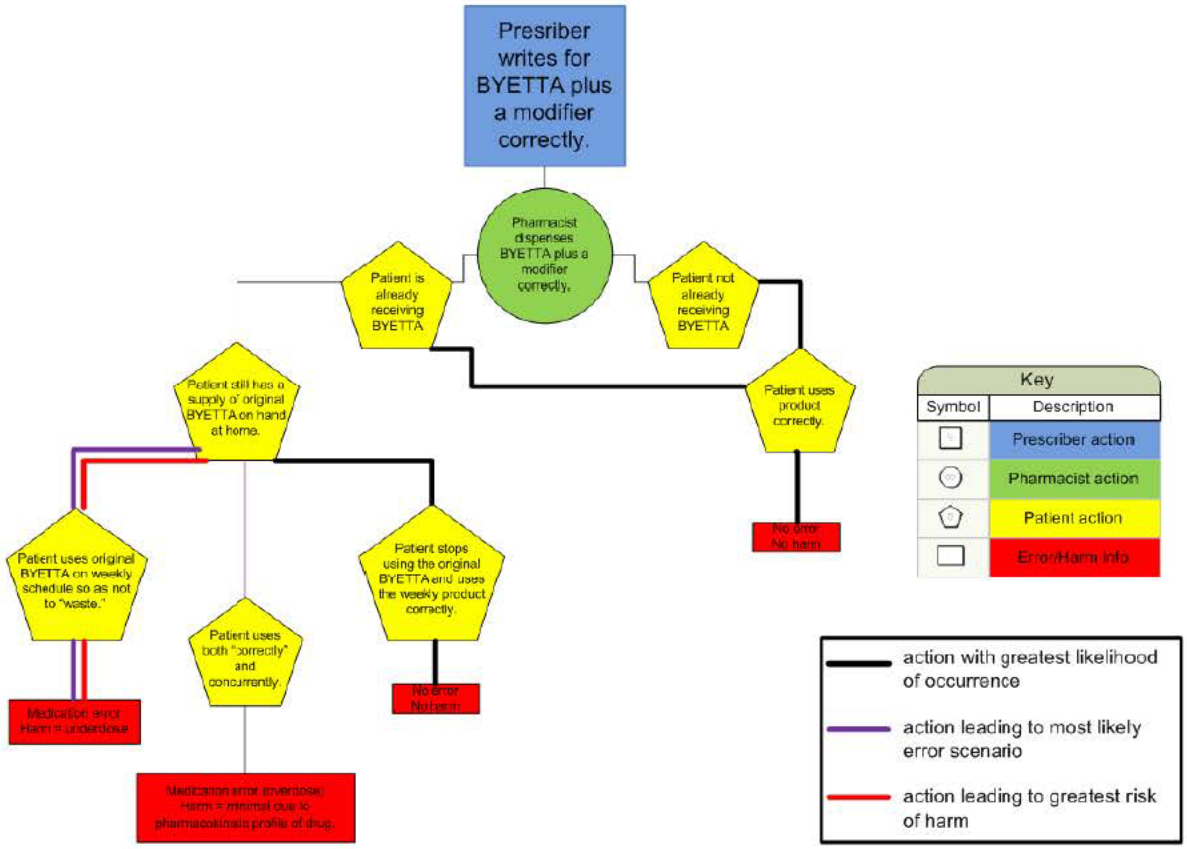
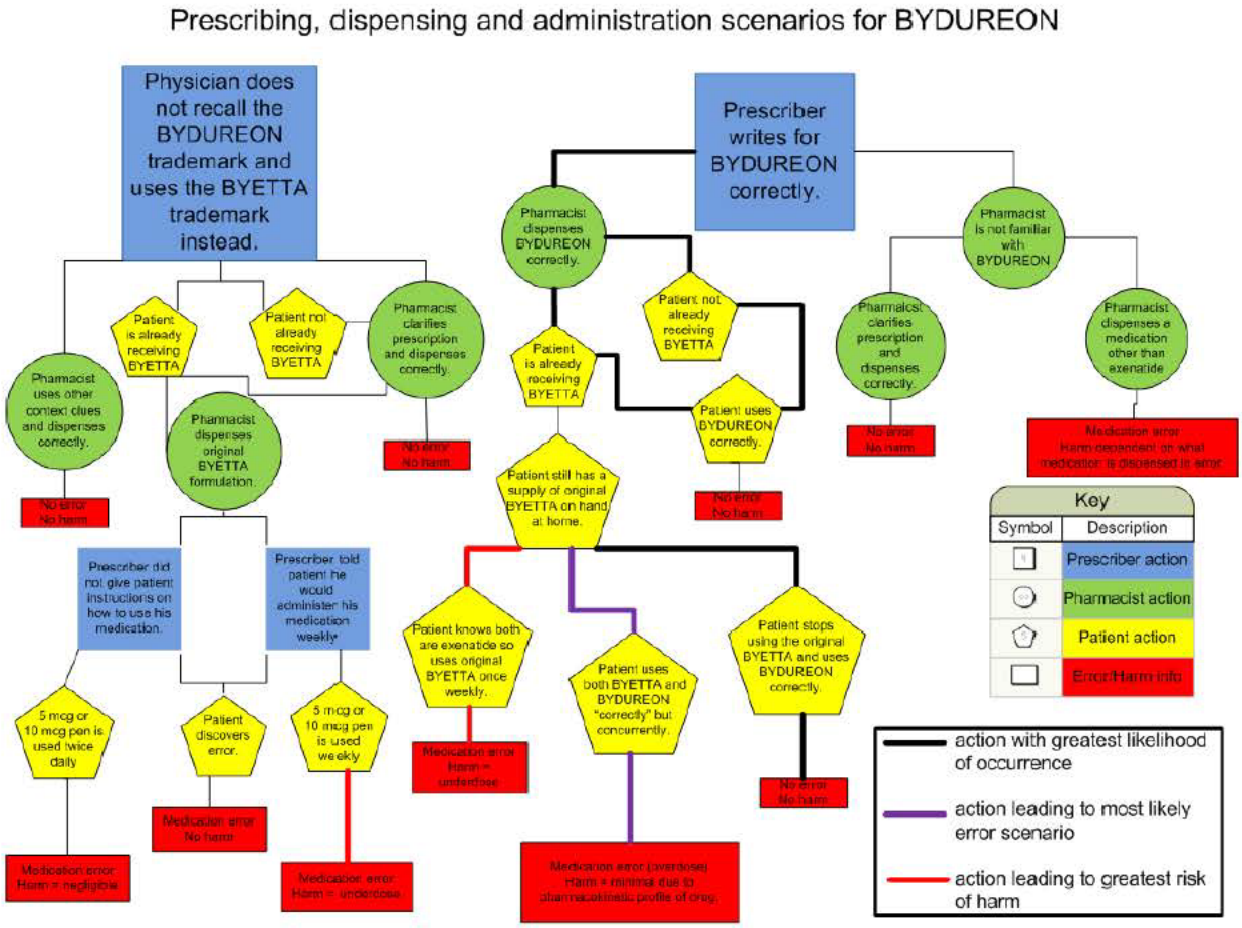


Table 4. Selective safety issues related to the use of the BYETTA plus a modifier naming convention*

BYETTA plus a modifier	
Pros	**Cons**
Less likely for practitioner to dispense both the weekly and twice-daily exenatide formulations because they will both have BYETTA in the trademark.	**Potential for confusion during product selection on computer screens (e.g., physician order entry screen, wholesaler order entry screen in pharmacy, order processing system in pharmacy)** **For example, products listed alphabetically by the "BYET" mnemonic :** **BYETTA 10 mcg** **BYETTA 5 mcg** **BYETTA plus modifier**
Less likely for patient to use both products because they will both have BYETTA in the trademark.	**If suffix is omitted, increased risk of confusion with original BYETTA product**
The BYETTA name may already be familiar to practitioners and patients and clues them in as to what the indication is for BYETTA.	More likely to mismatch strength or directions with the original BYETTA formulation
	Prescriber may forget what the actual modifier is and make up his own modifier. This could lead to confusion, a prescription that requires clarification, or the wrong formulation being dispensed.
	The dosage strength (2mg) may be confusing if practitioners assume this is a lower dose instead of a higher dose of BYETTA. Because the number 2 is less than the numbers 5 and 10 (original BYETTA formulation), when the dosage units are disregarded, the dosage strength of the weekly BYETTA formulation is counterintuitive.

***Bolded items indicate the issues considered to have the greatest significance.**

Figure 4


Prescribing, dispensing and administration scenarios for BYDUREON
Physician does not recall the BYDUREON trademark and uses the BYETTA trademark instead.
Pharmacist uses other context clues and dispenses correctly.
No error No harm
Patient is already receiving BYETTA
Patient not already receiving BYETTA
Pharmacist clarifies prescription and dispenses correctly.
No error No harm
Pharmacist dispenses original BYETTA formulation.
Prescriber did not give patient instructions on how to use his medication.
Prescriber told patient he would administer his medication weekly.
5 mcg or 10 mcg pen is used twice daily
Medication error Harm = negligible
Patient discovers error.
Medication error No harm
5 mcg or 10 mcg pen is used weekly
Medication error Harm = undertoxic
Prescriber writes for BYDUREON correctly.
Pharmacist dispenses BYDUREON correctly.
Patient is already receiving BYETTA
Patient still has a supply of original BYETTA on hand at home.
Patient knows both are exenatide so uses original BYETTA once weekly.
Medication error Harm = undertoxic
Patient uses both BYETTA and BYDUREON "correctly" but concurrently.
Medication error (overdose) Harm = minimal due to pharmacokinetic profile of drug
Patient stops using the original BYETTA and uses BYDUREON correctly.
No error No harm
Patient not already receiving BYETTA
Patient uses BYDUREON correctly.
No error No harm
Pharmacist is not familiar with BYDUREON
Pharmacist clarifies prescription and dispenses correctly.
No error No harm
Pharmacist dispenses a medication other than exenatide
Medication error Harm dependent on what medication is dispensed in error
Key
Symbol
Description
Prescriber action
Pharmacist action
Patient action
Error/Harm info
action with greatest likelihood of occurrence
action leading to most likely error scenario
action leading to greatest risk of harm

BYDUREON as a dual trademark	
Pros	**Cons**
Only available as one dosage strength; therefore prescriber would not need to indicate strength or directions and the correct product would still be dispensed.	**Practitioners and patients may not be familiar with a new product with a different trademark than BYETTA.**
Always administered weekly therefore decreasing confusion with BID dosing	**Increase risk that patient may get both BYETTA and BYDUREON due to name difference.**
The "DUR" portion gives a hint that it is a long-acting product	If patient is allergic to or intolerant of BYETTA he/she may not realize BYDUREON is the same active ingredient
	Injection "looks" different than the pen formulation of BYETTA increasing the risk that a patient may use both products at the same time because he doesn't recognize it as another exenatide formulation.
	Since the BYDUREON trademark would be unknown, there is potential for confusion with other trademarks on the market.
	Prescriber forgets the new trademark BYDUREON and calls it BYETTA (may or may not include a modifier with it).
	Practitioners are required to learn another trademark.

***Bolded items indicate the issues considered to have the greatest significance.**

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
IND-67092	GI-1	AMYLIN PHARMACEUTICALS INC	EXENATIDE LA (SYNTHETIC EXENDIN-4)INJECT
NDA-22200	ORIG-1	AMYLIN PHARMACEUTICALS INC	EXENATIDE LAR

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

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02/02/2010

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02/02/2010

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