

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

205649Orig1s000

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**

Proprietary Name Review

Date: November 20, 2013

Reviewer: Sarah K. Vee, PharmD, Safety Evaluator
Division of Medication Prevention and Analysis

Team Leader Yelena Maslov, PharmD, Team Leader
Division of Medication Prevention and Analysis

Drug Name and Strengths: Xigduo XR (Dapagliflozin and Metformin HCl
Extended-release) Tablets, 5 mg/500 mg, 5 mg/1000 mg,
10 mg/500 mg and 10 mg/1000 mg

Application Type/Number: NDA 205649

Applicant/sponsor: Astra Zeneca and Bristol-Myers Squibb

OSE RCM #: 2013-2528

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

CONTENTS

1	INTRODUCTION.....	1
2	METHODS AND DISCUSSION.....	1
3	CONCLUSIONS.....	1
3.1	Comments to the Applicant.....	1
4	References	2

1 INTRODUCTION

This review is a re-assessment of the proposed proprietary name, Xigduo XR, which DMEPA found acceptable in OSE Review #2013-292, dated July 16, 2013 under IND 106890.

2 METHODS AND DISCUSSION

For re-assessments of proposed proprietary names, DMEPA searches 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. For this review we used the same search criteria described in OSE Review 2013-292.

We note that none of the proposed product characteristics were altered. However, we evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which did not alter our previous conclusion regarding the acceptability of the proposed proprietary name. The searches of the databases did not yield any new names, thought to look similar to Xigduo XR and represent a potential source of drug name confusion.

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 updates. The Safety Evaluator did not identify any USAN stems in the proposed proprietary name, as of November 12, 2013. The Office of Prescription Drug Promotion (OPDP) re-reviewed the proposed name on November 7, 2013 and had no concerns regarding the proposed name from a promotional perspective.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Xigduo XR, did not identify any vulnerabilities that would result in medication errors with any additional names noted in this review. Thus, DMEPA has no objection to the proprietary name, Xigduo XR, for this product at this time.

If you have further questions or need clarifications, please contact Margarita Tossa, OSE project manager, at 301-796-4053.

3.1 COMMENTS TO THE APPLICANT

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

4 REFERENCES

1. **OSE Reviews 2013-292 Xigduo XR (Dapagliflozin and Metformin Extended Release) Proprietary Name Review_IND [Acceptable], Reasol S. Agustin, PharmD, July 16, 2013.**
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/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page?>)
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.

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

/s/

SARAH K VEE
11/20/2013

YELENA L MASLOV
11/21/2013

**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**

Proprietary Name Review

Date: July 16, 2013

Reviewer: Reasol S. Agustin, PharmD
Division of Medication Error Prevention and Analysis

Team Leader: Yelena Maslov, PharmD
Division of Medication Error Prevention and Analysis

Division Director: Carol Holquist, RPh
Division of Medication Error Prevention and Analysis

Drug Name and Strength: Xigduo XR (Dapagliflozin and Metformin HCl Extended-release) Tablets, 5 mg/500 mg, 5 mg/1000 mg, 10 mg/500 mg and 10 mg/1000 mg

Application Type/Number: IND 106890

Applicant/Sponsor: Astra Zeneca and Bristol-Myers Squibb

OSE RCM #: 2013-292

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

CONTENTS

1	INTRODUCTION.....	1
1.1	Regulatory History	1
1.2	Product Information.....	1
2.2	Safety Assessment.....	1
3	CONCLUSIONS.....	5
3.1	Comments to the Applicant.....	5
4	REFERENCES.....	6
	APPENDICES.....	9

1 INTRODUCTION

This review evaluates the proposed proprietary name, Xigduo XR, 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.

1.1 REGULATORY HISTORY

The Applicant, Astra Zeneca and Bristol-Myers Squibb submitted a request for review of the proposed proprietary name, Xigduo XR for Dapagliflozin and Metformin HCl Extended-release, on January 23, 2013 as part of IND 106890.

1.2 PRODUCT INFORMATION

The following product information is provided in the January 23, 2013 proprietary name submission.

- Active Ingredient: Dapagliflozin and Metformin Hydrochloride Extended-release
- Indication of Use: Adjunct to diet and exercise to improve glycemic control in adults with type 2 Diabetes Mellitus
- Route of Administration: Oral
- Dosage Form: Extended –release tablets
- Strength: 5 mg/500 mg, 5 mg/1000 mg, 10 mg/500 mg and 10 mg/1000 mg
- Dose and Frequency: 1 to 2 tablets by mouth once daily
- How Supplied: 30-count and 60-count bottles
- Storage: Store between 20 to 25°C
- Container and Closure Systems: May be packaged in Aluminum foil blisters with aluminum foil lidding or Heat induction sealed, high-density polyethylene (HDPE) bottles with a (b) (4) cap containing one silica gel desiccant canister/pouch.

2. RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Metabolism and Endocrinology Products concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The March 4, 2013 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The proposed proprietary name contains two components 1) the proposed root name, Xigduo and 2) the modifier XR. The Applicant indicated in their submission that the proposed name, Xigduo, has no derivation and the modifier 'XR' is intended to mean extended release. See Section 2.2.6

2.2.3 FDA Name Simulation Studies

Seventy-one practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. The most common misinterpretation in the inpatient study occurred with 19 participants misinterpreting the letter 'o' for 's' (i.e. 'XigduQ' misinterpreted as 'XigduS') and 9 participants misinterpreting the letter 'i' for 'r' (i.e. 'XIgduo' misinterpreted as XRgduo). Twenty-one of the 24 outpatient participants responded correctly and the most common misinterpretation occurred with 2 participants misinterpreting the letter 'o' for 's' and 't' (i.e. 'XigduQ' misinterpreted as 'XigduS' and 'XigduT'). None of the 24 voice participants responded correctly and a common misinterpretation occurred with 21 participants misinterpreting the letter 'X' for 'Z' (i.e. 'Xigduo' misinterpreted as 'Zigduo'). We have considered these variations in our look-alike and sound-alike searches and analysis (see Appendix B). See Appendix C for the complete listing of interpretation from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, February 11, 2013 e-mail, the Division of Metabolism and Endocrinology Products (DMEP) has no objections to the proposed name at the initial phase of the proprietary name review.

2.2.5 Failure Mode and Effects Analysis of Similar Names

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Xigduo XR. Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Xigduo XR identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Table 1 also includes the names identified by (b) (4) health not identified by DMEPA and require further evaluation.

Table 1: Collective List of Potentially Similar Names (DMEPA, Expert Panel Discussion (EPD), Other Disciplines, and External Name Study)					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Look Similar					
Xibrom	(b) (4)	Xifaxan	(b) (4)/EPD	Xigris	(b) (4)/EPD
Epiduo	EPD	Xofigo ^{***}	EPD	Xgeva	EPD
Xiaflex	EPD	Ximino	EPD	Zophix	EPD
Zohydro ER ^{***}	EPD	Zuplenz	EPD	(b) (4) ^{***}	EPD
(b) (4) ^{***}	EPD	Xcytrin	EPD	Zydis (Zyprexa)	SE
Zegerid	EPD	Xephrex	EPD	Tigan	EPD
Tegrin	EPD	Vi-q-tuss	EPD	Teslac	EPD
Zydone	SE	Zyclara	SE	Xylose	SE
Sound Similar					
Duac	(b) (4)	Epiduo	(b) (4)	Moxduo ^{***}	EPD
(b) (4) ^{***}	EPD				
Look and Sound Similar					
Zyprexa	(b) (4)	Xigduo ^{***}	EPD		

Our analysis of the 30 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined all thirty names will not pose a risk for confusion as described in Appendices D through E.

2.2.6 Analysis of Modifier XR

Our evaluation of the name Xigduo XR considered whether a modifier is necessary for this product. According to the Applicant, Xigduo XR is an extended-release tablet that should be administered once daily. Although there are no existing Xigduo products from which Xigduo XR would have to distinguish itself from, there are other immediate-release and extended-release metformin products currently in the market. Also, Xigduo XR is administered orally once daily whereas the immediate-release metformin products in the marketplace are typically administered twice daily. Thus, we evaluated whether or not a modifier is necessary for this product to signal the extended-release characteristics of the product. We also evaluated whether or not the lack of a modifier raises a potential safety concern, given the proposed dosage form.

^{***} This is proprietary and confidential information that should not be released to the public

We determined the Applicant needs a modifier based on the following:

First, we considered the extended-release properties of this product. We identified extended-release products approved without a modifier in the proprietary name and reviewed documented errors relating to wrong technique and wrong frequency of administration. Wrong technique errors involved patients or practitioners chewing, splitting, opening, or crushing the extended-release oral dosage forms when these products were intended to be administered intact. Wrong frequency errors involved the administration of the extended-release dosage form at intervals more frequent than labeled (e.g. taking a once daily drug twice a day). Wrong technique and wrong frequency errors occurred despite the presence of clear labeling directives to administer the products intact and at the given intervals. Additionally, based on the case narratives we were unable to determine a definitive root cause of the errors. These reports included extended-release products that had overlapping product strengths with immediate-release formulations.

We then considered whether the lack of a modifier may actually contribute to practitioners' and patients' knowledge deficit about the extended-release properties of the drug products. As it relates to this product, this consideration led us to evaluate whether the use a modifier in the name might help to avoid some of the wrong technique and wrong frequency errors.

With respect to wrong technique errors, we reviewed the Institute for Safe Medication Practices' (ISMP) list of "Oral Dosage Forms that Should Not be Crushed" to determine if a modifier exists that conveys an extended-release dosage form should not be divided, cut, crushed, or chewed. We focused our review on those names with modifiers that are commonly used to denote extended-release (eg., ER, SR, CR, XR, XL, and LA), since the Institute of Medicine has charged the FDA and Industry to standardize abbreviations to the greatest extent possible. Our review found this list contains a nearly equal number of extended-release drug products in which the proprietary name contains a modifier (n=82) to extended-release products with drug names without modifiers (n=84). Based on this information, we conclude there is no standard single modifier currently in the market today that is definitively linked to the requirement that an extended-release product should not be manipulated prior to administration. Although a clear pattern did not emerge from our review of this list with modifiers, our medication error postmarketing experience with drug products marketed without a modifier in the proprietary name leads us to believe that the failure to include a modifier that conveys the extended-release properties of the drug may predispose the product to wrong technique and wrong frequency errors. Therefore, in some circumstances, a modifier in the proprietary name of an extended-release product may help reduce the risk of these types of errors. In regards to this modifier,

As it relates to this product, the modifier "XR" has been used to communicate that a product is extended-release and may serve as a signal to healthcare practitioners that it differs from the currently marketed immediate-release metformin products on the market. DMEPA found the modifier XR has not been the source of confusion and is used consistently in the marketplace to mean extended-release for products that are dosed once daily. Since this product is also dosed once daily, XR is a reasonable modifier.

As a result, the presence of this modifier may trigger healthcare providers to consult the full prescribing information to determine how this product should be administered. We recognize there are limitations to this approach since there is postmarketing evidence that modifiers have been omitted or overlooked; however, given the risks associated with confusing this product with the immediate release products, we believe a modifier signaling the extended-release properties of this drug adds an incremental measure of safety.

Given the totality of factors considered above, we conclude a modifier “XR” is necessary for this product in order to help distinguish it from the currently marketed immediate-release metformin products in the marketplace.

2.2.7 Communication of DMEPA’s Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Metabolism and Endocrinology Products via e-mail on June 4, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Metabolism and Endocrinology Products on June 15, 2013, they stated no additional concerns with the proposed proprietary name, Xigduo XR.

3 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Margarita Tossa, OSE project manager, at 301-796-4053.

3.1 COMMENTS TO THE APPLICANT

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

Additionally, the proposed proprietary name must be submitted at the time of NDA submission. If any of the proposed product characteristics as stated in your January 23, 2013 submission are altered, the name must be resubmitted for review.

4 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. This database also lists the orphan drugs.

4. ***FDA Document 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.

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. ***U.S. Patent and Trademark Office*** (<http://www.uspto.gov>)

USPTO provides information regarding patent and trademarks.

8. ***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.

9. ***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.

10. ***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.

11. ***Access Medicine*** (www.accessmedicine.com)

Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

12. ***USAN Stems*** (<http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml>)

USAN Stems List contains all the recognized USAN stems.

13. ***Red Book*** (www.thomsonhc.com/home/dispatch)

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

14. ***Lexi-Comp*** (www.lexi.com)

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

15. ***Medical Abbreviations*** (www.medilexicon.com)

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

16. ***CVS/Pharmacy*** (www.CVS.com)

This database contains commonly used over the counter products not usually identified in other databases.

17. Walgreens (www.walgreens.com)

This database contains commonly used over the counter products not usually identified in other databases.

18. Rx List (www.rxlist.com)

RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

19. Dogpile (www.dogpile.com)

Dogpile is a [Metasearch](#) engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

20. Natural Standard (<http://www.naturalstandard.com>)

Natural Standard is a resource that aggregates and synthesizes data on complementary and alternative medicine.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by OPDP. OPDP evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. OPDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). 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

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

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. DMEPA considers the product characteristics associated with the proposed product 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.

¹ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/about/MedErrors.html>. Last accessed 10/11/2007.

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. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA 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.²

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA 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. DMEPA examines the phonetic similarity using patterns of speech. 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. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing 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).

² Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

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		
	<i>Potential Causes of Drug Name Similarity</i>	<i>Attributes Examined to Identify Similar Drug Names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> 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/Similar shape Upstrokes Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, DMEPA 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 searches 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. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses 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, DMEPA reviews 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. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Office of Prescription Drug Promotion (OPDP). We also consider input from other review disciplines (OND, ONDQA/OBP). 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 database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional 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 Simulation 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 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 record their interpretations of the orders which are recorded electronically.

4. Comments from Other Review Disciplines

DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

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

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

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, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their 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.³ 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

³ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

characteristics listed in Section 1.2 of this review. 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? And are there any components of the name that may function as a source of error beyond sound/look-alike?”

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 or because of some other component of the name. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess 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.

Moreover, 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 Overall Risk Assessment:

- a. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP’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 but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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 generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for 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 Applicant/Sponsor. However, the safety concerns set forth in criteria a through e above 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, confusing, or misleading 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 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: Letters and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Xigduo XR	Scripted May Appear as	Spoken May Be Interpreted as
‘X’	d, f, K, P, t, U, V, Y, Z	Z, S
lowercase ‘x’	a, d, skinny f, k, n, p, r, t, v, y	z, s
lowercase ‘i’	e, l, r	e
lowercase ‘g’	q, j, s, y	
lowercase ‘d’	cl, ci	
lowercase ‘u’	n, y, v, w, any vowel	
lowercase ‘o’	a, c, e, u, s, t, l	Oh
‘X’	d, f, K, P, t, U, V, Y	Z, S
‘R’	B, Pr, K	
Letter Strings		
‘ig’	ry	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Xigduo XR Study (Conducted on April 5, 2013)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> <p><i>Xigduo XR 10mg/1000mg T po daily</i></p>	<p>Xigduo XR 5 mg/1000 mg Take one by mouth daily #30</p>
<p><u>Outpatient Prescription:</u></p> <p><i>Xigduo XR 5/1000 T po #30</i></p>	

Study Name: Xigduo XR

192 People Received Study
71 People Responded

Study Name: Xigduo XR

Total	24	24	23	
INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
??? XR	0	1	0	1
VIGDUO XR	0	2	0	2
XEDUS XR	0	0	1	1
XEGDUO XR	0	0	1	1
XIGDUO	1	0	0	1
XIGDUO XR	1	0	0	1
XIGDUO XR	19	0	1	20
XIGDUS XR	1	0	6	7
XIGDUT XR	1	0	0	1
XIQDUO	1	0	0	1
XIRYDUS XR	0	0	1	1

XREGDUS XR	0	0	1	1
XREGUS	0	0	1	1
XREYDUS	0	0	1	1
XRGDUS XR	0	0	1	1
XRYDUO XR	0	0	1	1
XRYDUS XR	0	0	3	3
XRYDUS XT	0	0	1	1
XYDUS XR	0	0	4	4
ZADUOL XR	0	1	0	1
ZIDUO XR	0	2	0	2
ZIGDUAL XR	0	2	0	2
ZIGDUO XR	0	15	0	15
ZYGDUO XR	0	1	0	1

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described.

Proprietary Name		Active Ingredient	Similarity to Xigduo XR	Failure preventions
1	Zophix	Olanzapine	Look alike	International product marketed in Turkey
2	Zegerid	Omeprazole and Sodium Bicarbonate	Look alike	The pair have sufficient orthographic differences
3	Zyprexa	Ondansetron	Look alike and Sound alike	The pair have sufficient orthographic differences
4	Xcytrin		Look alike	Orphan drug. No pending NDA or commercial IND within the agency

5	(b) (4) ***	Calcitriol	Look alike	Proposed Proprietary Name was found unacceptable by DMEPA in OSE # (b) (4), dated (b) (4). Product approved under new proprietary name, Vectical.
6	(b) (4) ***	Linagliptin and Metformin	Sound alike	Proposed Proprietary Name was withdrawn by the Applicant on November 1, 2011. Product approved under new proprietary name, Jentaduetto
7	Duac	Benzoyl peroxide and Clindamycin	Sound alike	The pair have sufficient phonetic differences
8	Xigduo***	Dapagliflozin and Metformin	Look alike and Sound alike	This name is the subject of this review

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.

	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>		
<p>1 Zohydro ER^{***} (Hydrocodone Bitartrate)</p> <p>Dosage Form and Strength: Oral capsules: 10 mg, 20 mg, 30 mg, 40 mg, 50 mg</p> <p>Usual dose: 1 capsule by mouth every 12 hours (Patients will be dosed based on their pain level and opioid tolerance with a frequency of every 12 hours)</p>	<p>Orthographic similarity: The beginning letter ‘X’ and ‘Z’, letters ‘g’ and ‘y’, and the ending letter strings ‘duo’ and ‘dro’ appear orthographically similar when scripted.</p> <p>Dosage form and route of administration: Both are available as oral dosage forms</p>	<p>Orthographic difference: Zohydro contains an additional upstroke ‘h’ which is absent in Xigduo, giving the names different shapes.</p> <p>Strength: Both Xigduo XR and Zohydro ER are available in multiple strengths. Xigduo XR is a combination product that will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p>

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

<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>2 Zydone (Acetaminophen and Hydrocodone Bitartrate)</p> <p>Dosage Form and Strength: Oral Tablet: 400 mg/5 mg, 400 mg/7.5 mg, 400 mg/10 mg</p> <p>Usual dose: 1 to 2 tablets by mouth every 4 to 6 hours as needed</p>	<p>Orthographic similarity: The beginning letter strings ‘Xig’ and ‘Zy’ and ending letter strings ‘uo’ and ‘one’ appear orthographically similar when scripted. In addition, both names contain an upstroke ‘d’ in similar position.</p> <p>Dosage form and route of administration: Both are available as oral tablets</p>	<p>Frequency: Xigduo XR is prescribed once daily whereas Zydone is prescribed every 4 to 6 hours</p> <p>Strength: Both Xigduo XR and Zydone are available as combination products and in multiple strengths. Both products will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p>

	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Orthographic similarity: The beginning letter strings ‘Xig’ and ‘Zy’ appear orthographically similar when scripted. In addition, both names contain an upstroke ‘d’ in similar position.</p> <p>Dosage form and route of administration: Both are available as oral tablets</p> <p>Frequency: Both are prescribed once daily.</p>	<p>Orthographic similarity: The ending letter strings ‘uo’ and ‘is’ appear orthographically different when scripted. Although Xigduo contains 6 letters and Zydis contains 5 letters, Xigduo appears orthographically longer when scripted.</p> <p>Strength: Both Xigduo XR and Zyprexa Zydis are available in multiple strengths. Xigduo XR is a combination product that will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p>
<p>3</p> <p>Zyprexa Zydis (Olanzapine)</p> <p>Dosage Form and Strength: Oral dispersible tablet: 5 mg, 10 mg, 15 mg, 20 mg</p> <p>Usual dose: 5 to 20 mg by mouth once daily</p>	<p>4</p> <p>Xylose</p> <p>Dosage Form and Strength: Oral powder: 1 gm, 25 gm</p> <p>Usual dose: 5 or 25 gm dose in 200 to 300 mL of water</p>	<p>Orthographic similarity: The beginning letter strings ‘Xig’ and ‘Xy’ and the ending letter strings ‘uo’ and ‘ose’ appear orthographically similar when scripted. In addition, both names contain an upstroke ‘d’ and ‘l’ in similar positions.</p> <p>Dosage form and route of administration: Both are available as oral dosage forms</p> <p>Strength: Both Xigduo XR and Xylose are available in multiple strengths. Xigduo XR is a combination product that will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p>

	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Orthographic similarity: Both names begin with the letter string ‘Xi’</p>	<p>Orthographic difference: Xigduo contains a downstroke ‘g’ in position 3 and an upstroke ‘d’ in position 4 whereas Xibrom contains an upstroke ‘b’ in position 3, giving the names different shapes.</p> <p>Strength: Multiple vs. single. An order for Xigduo XR will require strength as it is available in multiple strengths vs. Xibrom is available in single strength and may be omitted. There is no numerical overlap or similarity between the strengths.</p> <p>Dose: 1 to 2 tablets vs. 1 drop</p>

	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>		
<p>6 Xigris* (Drotrecogin Alfa)</p> <p>Dosage Form and Strength: Powder for reconstitution: 5 mg/vial and 20 mg/vial</p> <p>Usual dose: 24 mcg/kg/hr over 96 hours. Based on actual body weight of 10 kg-70 kg: dose range 240 mcg to 1680 mcg (0.24 mg to 1.68 mg)</p> <p><i>*Product deactivated but generic still available</i></p>	<p>Orthographic similarity: Both begin with the letter string ‘Xig’</p>	<p>Orthographic difference: Xigduo contains an upstroke ‘d’ in position 4 which is absent in Xigris, giving the names different shapes.</p> <p>Strength: Both Xigduo XR and Xigris are available in multiple strengths. Xigduo XR is a combination product that will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p> <p>Dose: 1 to 2 tablets vs. xx mg</p> <p>Frequency: Xigduo XR is prescribed once daily whereas Xigris is prescribed once or over 96 hours.</p>

	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>		
<p>7 Epiduo (Benzoyl peroxide 2.5% and adapalene 0.1%)</p> <p>Dosage Form and Strength: Topical gel: 2.5%/0.1%</p> <p>Usual dose: Apply once daily</p>	<p>Orthographic similarity: Both names end with the letter string ‘duo’</p> <p>Frequency: Both are prescribed once daily</p>	<p>Orthographic difference: The beginning letter ‘X’ and ‘E’ appear orthographically different when scripted. In addition, Xigduo contains a downstroke ‘g’ in position 3 whereas Epiduo contains a downstroke ‘p’ in position 2, giving the names different shapes.</p> <p>Strength: Multiple vs. single. An order for Xigduo XR will require strength as it is available in multiple strengths vs. Xibrom is available in single strength and may be omitted. There is no numerical overlap or similarity between the strengths.</p> <p>Dose: 1 to 2 tablets vs. apply</p>

<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>8 Ximino (Minocycline)</p> <p>Dosage Form and Strength: Oral extended-release capsule: 45 mg, 67.5 mg, 90 mg, 112.5 mg, 135 mg</p> <p>Usual dose: 1 capsule by mouth once daily (1 mg/kg once daily for patients age 12 years and older)</p>	<p>Orthographic similarity: Both names begin with the letter string ‘Xi’ and end with the letter ‘o’</p> <p>Dosage form and route of administration: Both are available as oral dosage forms</p> <p>Frequency: Both are prescribed once daily</p>	<p>Orthographic difference: Xigduo contains a downstroke ‘g’ in position 3 and an upstroke ‘d’ in position 4 which is absent in Ximino, giving the names different shapes.</p> <p>Strength: Strength: Both Xigduo XR and Ximino are available in multiple strengths. Xigduo XR is a combination product that will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p>

	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Orthographic similarity: Both names begin with the letter ‘X’ and end with the letter ‘o’</p>	<p>Orthographic difference: Xigduo contains a downstroke ‘g’ in position 3 and an upstroke ‘d’ in position 4 whereas Xofigo contains an upstroke/downstroke ‘f’ in position 3 and a downstroke ‘g’ in position 5, giving the names different shapes.</p> <p>Strength: Multiple vs. single. An order for Xigduo XR will require strength as it is available in multiple strengths vs. Xofigo is available in single strength and may be omitted.</p> <p>Frequency: Xigduo XR is prescribed once daily whereas Xofigo is prescribed ever 4 weeks</p> <p>Dose: 1 to 2 tablets vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie.</p>

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

	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>		
<p>10 Xgeva (Denosumab)</p> <p>Dosage Form and Strength: Subcutaneous solution: 60 mg/mL and 120 mg/1.7 mL</p> <p>Usual dose: Inject 60 mg subcutaneously every 6 months or 120 mg subcutaneously every 4 weeks</p>	<p>Orthographic similarity: Both names begin with the letter ‘X’ and contain the downstroke ‘g’ in similar positions. In addition, the ending letter strings ‘uo’ and ‘va’ appear orthographically similar when scripted.</p>	<p>Orthographic difference: Xigduo contains an upstroke ‘d’ in position 4 which is absent on Xgeva, giving the names different shapes.</p> <p>Strength: Both Xigduo XR and Xgeva are available in multiple strengths. Xigduo XR is a combination product that will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p> <p>Frequency: Xigduo XR is prescribed once daily whereas Xgeva is prescribed every 6 months or every 4 weeks</p> <p>Dose: 1 to 2 tablets vs. 60 mg or 120 mg</p>

<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>11 Xiaflex (Collagenase Clostridium Histolyticum)</p> <p>Dosage Form and Strength: Injection solution reconstituted: 0.9 mg</p> <p>Usual dose: 0.58 mg per injection into a palpable cord with a contracture of an MP joint or a PIP joint</p>	<p>Orthographic similarity: Both names begin with the letter string ‘Xi.’ The letter ‘g’ and letter string ‘af’ appear orthographically similar when scripted. In addition, both names contain an upstroke ‘d’ and ‘l’ in similar positions.</p>	<p>Strength: Multiple vs. single. An order for Xigduo XR will require strength as it is available in multiple strengths vs. Xiaflex is available in single strength and may be omitted. There is no numerical overlap or similarity between the strengths.</p> <p>Frequency: Xigduo XR is prescribed once daily whereas Xiaflex is prescribed once</p> <p>Dose: 1 to 2 tablets vs. 0.58 mg</p>

<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>12 Tegrin (Coal Tar)</p> <p>Dosage Form and Strength: Topical cream, liquid, and shampoo</p> <p>Usual dose: Use as directed</p>	<p>Orthographic similarity: The beginning letter string ‘Xig’ and ‘Teg’ appear orthographically similar when scripted.</p>	<p>Orthographic difference: Xigduo contains an upstroke ‘d’ in position 4 which is absent in Tegrin, giving the names different shapes.</p> <p>Strength: An order for Xigduo XR will require strength as it is available in multiple strengths vs. Tegrin does not have strength.</p> <p>Dosage form and route of administration: Xigduo is available as an oral tablet whereas Tegrin is available as a topical cream, liquid, or shampoo which needs to be specified for a complete prescription.</p> <p>Dose: 1 to 2 tablets vs. use as directed</p>

<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>13 Xifaxan (Rifaximin)</p> <p>Dosage Form and Strength: Oral tablet: 200 mg, 550 mg</p> <p>Usual dose: 550 mg by mouth 2 times a day or 200 mg by mouth 3 times a day for 3 days.</p>	<p>Orthographic similarity: Both names begin with the letter string ‘Xi’</p> <p>Dosage form and route of administration: Both are available as oral dosage tablets</p>	<p>Orthographic difference: Xigduo contains an upstroke ‘d’ in position 4 which is absent in Xifaxan, giving the names different shapes.</p> <p>Strength: Strength: Both Xigduo XR and Xifaxan are available in multiple strengths. Xigduo XR is a combination product that will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p>

	<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>14</p>	<p>Vi-Q-tuss (Guaifenesin and Hydrocodone)</p> <p>Dosage Form and Strength: Oral syrup: 100 mg-5 mg/5 mL</p> <p>Usual dose: 5 to 15 mL by mouth every 4 to 6 hours as needed</p>	<p>Orthographic similarity: The beginning letter strings ‘Xig’ and ‘Viq’ (if written together) appear orthographically similar when scripted.</p> <p>Dosage form and route of administration: Both are available as oral dosage forms</p>	<p>Orthographic difference: Even though both names contain an upstroke in position 4, the letter strings ‘duo’ and ‘tuss’ appear orthographically different when scripted.</p> <p>Strength: Both Xigduo XR and Vi-Q-tuss are available in multiple strengths. Xigduo XR is a combination product that will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p> <p>Frequency: Xigduo XR is prescribed once daily whereas Vi-q-tuss is prescribed every 4 to 6 hours</p> <p>Dose: 1 to 2 tablets vs. 5 to 15 mL</p>

<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>15 Zyclara (Imiquimod)</p> <p>Dosage Form and Strength: External cream: 3.75%</p> <p>Zyclara Pump: 2.5%, 3.75%</p> <p>Usual dose: 2 (3.75% or 2.5%) packets or full actuations of the pump per application</p>	<p>Orthographic similarity: The beginning letter strings ‘Xig’ and ‘Zy’ and the letter ‘d’ and ‘cl’ appear orthographically similar when scripted.</p> <p>Frequency: Both are prescribed once daily</p>	<p>Strength: Strength: Both Xigduo XR and Zyclara are available in multiple strengths. Xigduo XR is a combination product that will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p> <p>Dose: 1 to 2 tablets vs. 2 packets or full actuations</p>

<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
<p>16 Tigan (Trimethobenzamide)</p> <p>Dosage Form and Strength: Oral capsule: 300 mg Intramuscular solution: 100 mg/mL</p> <p>Usual dose: 300 mg 3 or 4 times daily</p>	<p>Orthographic similarity: The beginning letter string ‘Xig’ and ‘Teg’ appear orthographically similar when scripted.</p>	<p>Orthographic difference: Xigduo contains an upstroke ‘d’ in position 4 which is absent in Tigan, giving the names different shapes.</p> <p>Strength: Both Xigduo XR and Tigan are available in multiple strengths. Xigduo XR is a combination product that will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p> <p>Dosage form and route of administration: Xigduo is available as an oral dosage form whereas Tigan is available as an oral dosage form or as an intramuscular solution, which needs to be specified for a complete prescription.</p> <p>Frequency: Xigduo XR is prescribed once daily whereas Tigan is prescribed 3 or 4 times daily.</p>

	<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
17	<p>Teslac (Testolactone)</p> <p>Dosage Form and Strength: Oral tablet: 50 mg</p> <p>Usual dose: 1 to 2 tablets by mouth 4 times daily</p>	<p>Orthographic similarity: The beginning letter strings ‘Xig’ and ‘Tes’ appear orthographically simila when scripted.</p> <p>Dosage form and route of administration: Both are available as oral tablets</p>	<p>Orthographic difference: Even though both names contain an upstroke ‘d’ / ‘l’ in similar positions, the letters appear orthographically different when scripted.</p> <p>Strength: Both Xigduo XR and Teslac are available in multiple strengths. Xigduo XR is a combination product that will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p>

	<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
18	(b) (4)		

	<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
19	<p>Zuplenz (Ondansetron)</p> <p>Dosage Form and Strength: Oral film: 4 mg, 8 mg</p> <p>Usual dose: 24 mg orally, given 30 minutes before chemotherapy; 8 mg by mouth 2 to 3 times daily</p>	<p>Orthographic similarity: The beginning letter strings ‘Xig’ and ‘Zup’ appear orthographically similar when scripted. In addition, both names contain an upstroke ‘d’ and ‘l’ in similar positions.</p> <p>Dosage form and route of administration: Both are available as oral dosage forms</p>	<p>Orthographic difference: The ending letter strings ‘uo’ and ‘enz’ appear orthographically different when scripted</p> <p>Strength: Both Xigduo XR and Zuplenz are available in multiple strengths. Xigduo XR is a combination product that will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p>

	<p>Proposed name: <i>Xigduo XR</i> (Dapagliflozin and Metformin XR)</p> <p>Dosage form and Strength: Oral tablets: 5 mg/500 mg, 10 mg/500 mg, 5 mg/1000 mg, and 10 mg/1000 mg</p> <p>Usual dose: 1 to 2 tablets by mouth once daily</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p> <p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p> <p>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
20	<p>Moxduo*** (Morphine sulfate and Oxycodone HCl)</p> <p>Dosage Form and Strength: Oral capsules: 3 mg/2 mg, 6 mg/4 mg, 9 mg/6 mg, 12 mg/8 mg</p> <p>Usual dose: 1 or 2 capsules by mouth every 4 to 6 hours</p>	<p>Orthographic similarity: Both names end with the letter string ‘duo’</p> <p>Phonetic similarity: Both names contain three syllables. The last 2 syllables ‘du-oh’ sound phonetically similar when spoken</p> <p>Dosage form and route of administration: Both are available as oral dosage forms</p>	<p>Orthographic difference: The beginning letter strings ‘Xig’ and ‘Mox’ appear orthographically different when scripted.</p> <p>Phonetic difference: The first syllables ‘Zig’ vs. ‘Mox’ sound phonetically different when spoken</p> <p>Strength: Both Xigduo XR and Moxduo are combination products and are available in multiple strengths. Both products will require both strengths for a complete prescription. There is no numerical overlap or similarity between the strengths during prescription writing</p> <p>Frequency: Xigduo XR is prescribed once daily whereas Moxduo is prescribed every 4 to 6 hours</p>

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

/s/

REASOL AGUSTIN
07/16/2013

YELENA L MASLOV
07/16/2013

CAROL A HOLQUIST
07/16/2013