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RESEARCH**

APPLICATION NUMBER:

203971Orig1s000

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: March 29, 2013

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Drug Name and Strength: Xofigo (Radium Ra 223 Dichloride) Injection
1,000 kBq/mL (27 microcurie/mL)

Application Type/Number: NDA 203971

Applicant: Bayer HealthCare Pharmaceuticals Inc.

OSE RCM #: 2013-148

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

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Xofigo, 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

Xofigo (Radium Ra 223 Dichloride) proprietary name was found conditionally acceptable in October 21, 2011 in OSE Review 2011-1417 during the IND phase. The Applicant submitted the NDA on December 14, 2012. Additionally, on January 10, 2013, the Applicant submitted a proprietary name request for Xofigo, which is the subject of this review. Since the last review, the radioactivity concentration per mL was ^{(b) (4)} 27 microcurie/mL (see *section 1.2 Product Information*).

1.2 PRODUCT INFORMATION

The following product information is provided in the January 10, 2013 proprietary name submission.

- Active Ingredient: Radium Ra 223 Dichloride
- Indication of Use: therapeutic alpha particle-emitting pharmaceutical for the treatment of castration-resistant prostate cancer patients with bone metastases
- Route of Administration: Intravenous
- Dosage Form: Injection
- Strength: 1,000 kBq/mL or 27 microcurie/mL at the reference date
- Dose and Frequency: 50 kBq/kg or 1.35 microcurie/kg every 4 weeks for 6 injections
- How Supplied: single-dose vials containing 6 mL of solution
- Storage: Do not store above 40°C (104°F). Store in the original container or equivalent radiation shielding.
- Container and Closure System: glass vial

Additionally, the US Nuclear Regulatory Commission (NRC) has determined that Xofigo (Radium Ra 223 Dichloride) licensing under 10 CFR 35.40 “Unsealed Byproduct Material – Written Directive Required” is appropriate. Thus, this product will be managed by nuclear pharmacists, authorized physician, nuclear medicine technologist or physician authorized user. The *Written Directive* is documentation filled out by the authorized user of the nuclear pharmaceutical product whose purpose is to verify the correct patient, drug, dose, and route of administration.

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 Oncology Products I (DOP1) 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 February 8, 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 Applicant indicated in their submission that the proposed name, Xofigo, is an invented word without any special meaning. This proprietary name is comprised of a single word that does not contain any components (i.e., a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 FDA Name Simulation Studies

Eighty-eight practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. In the Inpatient Study, only two of the 23 responses were misinterpreted. There were no specific trends noted in the misinterpretations of the Outpatient Study. All the misinterpretations in the Voice Study were the letter 'Z' for the letter 'X'. See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, January 30, 2013 e-mail, the DOP1 did not forward any comments or concerns relating 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, Xofigo. Table 1 lists the names identified by the primary reviewer and the Expert Panel Discussion (EPD) in this review cycle to have potential orthographic, phonetic, or spelling similarity to the proposed proprietary name,

Xofigo. Table 1 also includes the names identified from the FDA Prescription Simulation Studies and the (b) (4) external study that were not identified by DMEPA and require further evaluation. Appendices G and H contain the list of the names previously identified and evaluated in OSE Review 2011-1417. These names were re-reviewed due to (b) (4)

However, we still agree with the previous review's conclusions, thus none of the previously reviewed names are of concern.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, and External Name Study)					
Look Similar					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
(b) (4)	EPD	Exforge	External	Fortaz	Safety Evaluator
(b) (4)	Safety Evaluator	Keflex	External	(b) (4)	Safety Evaluator
Kefzol	External	Kof-eze	EPD	Koflet	EPD
Lofibra	EPD	Potiga	EPD	Toposar	EPD
Vaniqa	EPD	Xalkori	EPD	Xeloda	EPD
Xiaflex	EPD	Xifaxan	EPD	Xifizia	EPD
Xobaline	EPD	Xotopo	EPD	Zolinza	SE
Zytopic	Safety Evaluator				
Sound Similar					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Zomig	Safety Evaluator	Zovia	Safety Evaluator		
Look and Sound Similar					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Forfivo XL	SE	PhosLo	External	Xgeva	SE
Xigris	External	(b) (4)	EPD	Xofigo	EPD
Xolair	EPD, External	Xolegel	EPD, External	Xopenex	EPD, External
Xtandi	SE	Zofran	External	Zoloft	External
Zometa	External	Zytiga	SE	Exalgo	SE

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Our analysis of the 39 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined 39 names will not pose a risk for confusion as described in Appendices D through F.

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the DOP1 via e-mail on February 25, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DOP1 on March 14, 2013, they stated no additional concerns with the proposed proprietary name, Xofigo.

3 CONCLUSIONS

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

If you have questions or need clarifications, please contact Francis Fahnbulleh, OSE project manager, at 301-796-0942.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Xofigo, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your January 10, 2013 submission are altered, the name must be resubmitted for review.

Additionally, the proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The conclusions upon re-review are subject to change.

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/aboutMedErrors.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

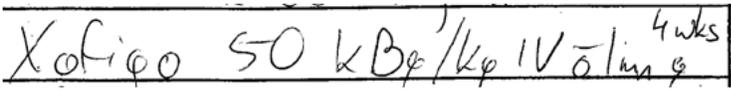
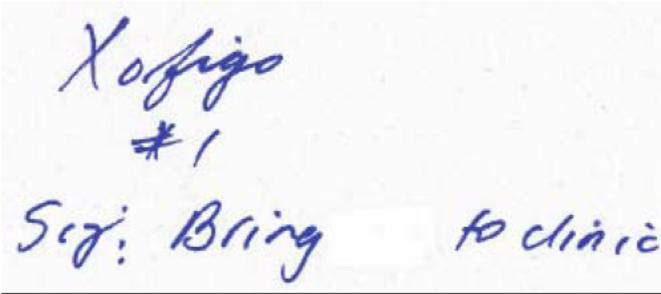
past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors' have changed a product's proprietary name in the post-approval 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,	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'X'	H, K, V, Y, Z	C, S, Z
lowercase 'x'	f, n, y, z	c, s, z
lowercase 'o'	a, s, u	a, u
lowercase 'f'	b, t, x	ph, v
lowercase 'i'	e, l	a, e, ee, y
lowercase 'g'	j, p, q, y, z	c, k
Letter strings		
of	olf, orf	
fi	br	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Xofigo Study (Conducted on 1/31/2013)

Handwritten Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p>  <p><u>Outpatient Prescription:</u></p> 	<p>Xofigo</p> <p>Bring to Clinic</p> <p>Quantity # 1</p>

FDA Prescription Simulation Responses

Study Name: Xofigo

As of Date 2/14/2013

192 People Received Study
88 People Responded

Study Name: Xofigo

	Total	25	33	30	
INTERPRETATION	INPATIENT	VOICE	OUTPATIENT	TOTAL	
Xofigo	23	0	19	42	
Xofigs	0	0	2	2	
Xofio	1	0	0	1	
Xofoqo	1	0	0	1	
Xofrigo	0	0	3	3	
Xolfigo	0	0	2	2	
Xorfigo	0	0	3	3	
Zofeego	0	2	0	2	
Zofego	0	6	0	6	
Zofigo	0	17	1	18	
Zophego	0	1	0	1	
Zophigo	0	3	0	3	
Zophygo	0	1	0	1	
Zoseego	0	1	0	1	
Zovego	0	1	0	1	
Zovigo	0	1	0	1	

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

No.	Proprietary Name	Active Ingredient	Similarity to Xofigo	Failure preventions
1.	(b) (4)			
2.	Kof-eze	Menthol	Look	Product is for veterinary medicine.
3.	Toposar	Etoposide	Look	The pair have sufficient orthographic and/or phonetic differences.
4.	Xifizia		Look	Name identified in USPTO database. Unable to find product characteristics in commonly used drug databases.
5.	Xotopo		Look	Name identified in USPTO database. Unable to find product characteristics in commonly used drug databases.
6.	(b) (4)		Look and Sound	Name identified in USPTO database. Unable to find product characteristics in commonly used drug databases. (b) (4)
7.	Xofigo	Radium Ra 223 Dichloride	Look and Sound	Subject of this review.

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Appendix E: Proprietary names determined in OSE Review 2011-1417 not likely to lead to a medication error.

No.	Proprietary Name	Active Ingredient	Similarity to Xofigo
1.	Keflex	Cephalexin	Look
2.	Kefzol	Cefazolin	Look
3.	Xiaflex	Collagenase Clostridium Histolyticum	Look
4.	Forfivo XL	Bupropion	Look and Sound
5.	PhosLo	Calcium Acetate	Look and Sound
6.	Xigris	Drotrecogin Alfa (activated)	Look and Sound
7.	Xolair	Omalizumab	Look and Sound
8.	Xolegel	Ketoconazole	Look and Sound
9.	Zofran	Ondansetron	Look and Sound
10.	Zoloft	Sertraline	Look and Sound
11.	Zometa	Zoledronic Acid	Look and Sound
12.	Exalgo	Hydromorphone	Look and Sound

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

No.	<p>Xofigo (Radium Ra 223 Dichloride Injection) 1,000 kBq/mL (27 microcurie/mL) Usual Dose: 50 kBq/kg (3,000 kBq to 6,000 kBq) or 1.35 microcurie/kg (81 microcurie to 162 microcurie) every 4 weeks for 6 injections</p>	<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion Causes (could be multiple)</p>	<p>Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</p>
1.	<p style="text-align: right;">(b) (4)</p>		
2.	<p>Exforge (Amlodipine and Valsartan) 5 mg/160 mg, 5 mg/320 mg, 10 mg/160 mg, 10 mg/320 mg tablets Usual Dose: 1 tablet orally once daily</p>	<p>Orthographic similarities - Both names share identical downstroke letters in similar positions ('f', 'g')</p>	<p>Orthographic differences - The beginning of both names differ ('Ex-' vs. 'Xo-')</p> <p>Differing product characteristics - Dose: 1 tablet vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie - Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.</p>

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No.	<p>Xofigo (Radium Ra 223 Dichloride Injection)</p> <p>1,000 kBq/mL (27 microcurie/mL)</p> <p>Usual Dose: 50 kBq/kg (3,000 kBq to 6,000 kBq) or 1.35 microcurie/kg (81 microcurie to 162 microcurie) every 4 weeks for 6 injections</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>
3.	<p>Fortaz (Ceftazidime)</p> <p>500 mg, 1 gm, 2 gm, 6 gm (bulk)</p> <p>Usual Dose: 250 mg to 2 g intravenously every 8 to 12 hours</p>	<p>Orthographic similarities</p> <ul style="list-style-type: none"> - Both name share letters that appear similar when scripted ‘Fo-’ vs. ‘Xo-’ - Both name share upstroke letter in similar position (‘f’ vs. ‘t’) - Both names share a downstroke letter in similar positions (‘z’ vs. ‘g’) <p>Overlapping product characteristics</p> <ul style="list-style-type: none"> - Intravenous Administration - Similar strength: 1,000 mg vs. 1,000 kBq 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Fortaz contains an additional letter - Xofigo contains an additional letter (‘o’) after the downstroke letter at the end of the name <p>Differing product characteristics</p> <ul style="list-style-type: none"> - Dose: 250 mg to 2 g vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie - Although the strengths may be numerically similar, the units of measure differ (mg vs. kBq) - Frequency of Administration: every 8 to 12 hours vs. every 4 weeks - Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.

No.	<p>Xofigo (Radium Ra 223 Dichloride Injection)</p> <p>1,000 kBq/mL (27 microcurie/mL)</p> <p>Usual Dose: 50 kBq/kg (3,000 kBq to 6,000 kBq)</p> <p>or</p> <p>1.35 microcurie/kg (81 microcurie to 162 microcurie) every 4 weeks for 6 injections</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>
4.	<div style="text-align: right;">(b) (4)</div>		

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No.	<p>Xofigo (Radium Ra 223 Dichloride Injection)</p> <p>1,000 kBq/mL (27 microcurie/mL)</p> <p>Usual Dose: 50 kBq/kg (3,000 kBq to 6,000 kBq) or 1.35 microcurie/kg (81 microcurie to 162 microcurie) every 4 weeks for 6 injections</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>
5.	<p>Koflet Herbal Lozenge</p> <p>Usual Dose: Dissolve 1 lozenge in mouth 3 to 4 times daily</p>	<p>Orthographic similarities</p> <ul style="list-style-type: none"> - Both names share letters that appear similar when scripted ('Kofl-' vs. 'Xofi-') 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - The endings of the names differ ('-let' vs. '-go') mainly due to the downstroke 'g' in Xofigo. <p>Differing product characteristics</p> <ul style="list-style-type: none"> - Dose: 1 lozenge vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie - Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.
6.	<p>Lofibra (Fenofibrate)</p> <p>54 mg, 160 mg tablet 67 mg, 134 mg, 200 mg capsules</p> <p>Usual Dose: 1 tablet orally daily</p>	<p>Orthographic similarities</p> <ul style="list-style-type: none"> - Both names share identical letters in the same position ('ofi-' vs. 'ofi-') - Similar dose overlap: 134 mg and 160 mg vs. 134 microcurie and 160 microcurie 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - The initial letters differ ('X' vs. 'L'). - The endings differ ('-bra' vs. '-go') <p>Differing product characteristics</p> <ul style="list-style-type: none"> - Dose: 1 tablet vs. 3,000 kBq to 6,000 kBq - Although the doses may be numerically similar, the units of measure differ (mg vs. microcurie) - Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.

No.	<p>Xofigo (Radium Ra 223 Dichloride Injection)</p> <p>1,000 kBq/mL (27 microcurie/mL)</p> <p>Usual Dose: 50 kBq/kg (3,000 kBq to 6,000 kBq) or 1.35 microcurie/kg (81 microcurie to 162 microcurie) every 4 weeks for 6 injections</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>
7.	<p>Potiga (Ezogabine)</p> <p>50 mg, 200 mg, 300 mg, 400 mg tablets</p> <p>Usual Dose: 1 tablet orally 3 times daily</p>	<p>Orthographic similarities</p> <ul style="list-style-type: none"> - Both names share identical letters in the same position: ('o', '-ig-') - Both names share letters that appear similar when scripted ('P' vs. 'X', 't' vs. 'f', 'a' vs. 'o') <p>Overlapping product characteristics</p> <ul style="list-style-type: none"> - Numerically similar dose: 150 mg vs. 150 microcurie 	<p>Differing product characteristics</p> <ul style="list-style-type: none"> - Dose: 1 tablet (50 mg, 200 mg, 300 mg, 400 mg) vs. 3,000 kBq to 6,000 kBq - Although the doses may be numerically similar, the units of measure differ (mg vs. microcurie) - Frequency of Administration: 3 times daily vs. every 4 weeks - Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.
8.	<p>Vaniqa (Eflornithine HCl)</p> <p>13.9% cream</p> <p>Usual Dose: Apply a thin layer to affected area of face twice daily at least 8 hours apart</p>	<p>Orthographic similarities</p> <ul style="list-style-type: none"> - Both names share letters in the same position that appear similar when scripted ('Va-' vs. 'Xo-', '-iqa' vs. '-igo') 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Xofigo contains an upstroke letter (f) in the middle of the name. Additionally, depending on how it is written, the 'f' may appear as a crossstroke and/or downstroke letter as well. <p>Differing product characteristics</p> <ul style="list-style-type: none"> - Dose: thin layer vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie - Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.

No.	<p>Xofigo (Radium Ra 223 Dichloride Injection)</p> <p>1,000 kBq/mL (27 microcurie/mL)</p> <p>Usual Dose: 50 kBq/kg (3,000 kBq to 6,000 kBq) or 1.35 microcurie/kg (81 microcurie to 162 microcurie) every 4 weeks for 6 injections</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>
9.	<p>Xalkori (Crizotinib)</p> <p>200 mg, 250 mg capsule</p> <p>Usual Dose: 1 tablet twice daily</p>	<p>Orthographic similarities</p> <ul style="list-style-type: none"> - Both names share letters in the same position that appear similar when scripted ('Xal-' vs. 'Xof-') <p>Overlapping product characteristics</p> <ul style="list-style-type: none"> - Similar patient population: oncology patients 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Xalkori contains an additional upstroke letter ('k'). - The endings of the names differ ('-kori' vs. '-igo') <p>Differing product characteristics</p> <ul style="list-style-type: none"> - Dose: 1 tablet (200 mg, 250 mg) vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie - Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.
10.	<p>Xeloda (Capecitabine)</p> <p>150 mg, 500 mg tablet</p> <p>Usual Dose: 1,250 mg/m² twice daily (morning and evening; equivalent to 2,500 mg/m² total daily dose) for 2 weeks. After a 1-week rest period, repeat this 3-week cycle.</p> <p>1750 mg to 3000 mg</p>	<p>Orthographic similarities</p> <ul style="list-style-type: none"> - Both names share letters in the same position that appear similar when scripted ('Xel-' vs. 'Xof-', '-a' vs. '-o') <p>Numerically similar dose: 3,000 mg vs. 3,000 kBq</p> <p>Overlapping product characteristics</p> <ul style="list-style-type: none"> - Similar patient population: oncology patients 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Xeloda contains an upstroke letter ('d') in the same position that Xofigo contains a downstroke letter ('g') <p>Differing product characteristics</p> <ul style="list-style-type: none"> - Although the doses may be numerically similar, the units of measure differ (mg vs. kBq) - Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.

No.	<p>Xofigo (Radium Ra 223 Dichloride Injection)</p> <p>1,000 kBq/mL (27 microcurie/mL)</p> <p>Usual Dose: 50 kBq/kg (3,000 kBq to 6,000 kBq) or 1.35 microcurie/kg (81 microcurie to 162 microcurie) every 4 weeks for 6 injections</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>
11.	<p>Xifaxan (Rifaximin)</p> <p>200 mg, 550 mg tablets</p> <p>Usual Dose: 200 mg orally 3 times daily 550 mg orally 2 times daily</p>	<p>Orthographic similarities</p> <p>- Both names share letters in the same position that appear similar when scripted (‘Xif-’ vs. ‘Xof-’)</p>	<p>Orthographic differences</p> <p>- The endings of the name differ (‘-axan’ vs. ‘-igo’) mainly due to the downstroke letter (‘g’) in Xofigo.</p> <p>Differing product characteristics</p> <p>- Dose: 200 mg, 550 mg vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie</p> <p>- Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.</p>
12.	<p>Xobaline (Folic Acid 800 mg and Vitamin B12)</p> <p>800 mcg/200 mcg tablets</p> <p>Usual Dose: 1 tablet orally daily</p>	<p>Orthographic similarities</p> <p>- Both names share letters in the same position that appear similar when scripted (‘Xob-’ vs. ‘Xof-’)</p>	<p>Orthographic differences</p> <p>- The endings of the name differ (‘-aline’ vs. ‘-igo’) mainly due to upstroke letter (‘l’) in Xobaline and the downstroke letter (‘g’) in Xofigo.</p> <p>Differing product characteristics</p> <p>- Dose: 1 tablets vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie</p> <p>- Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.</p>
13.	<p>Zolinza (Vorinostat)</p> <p>100 mg capsule</p> <p>Usual Dose: 2 to 4 tablets (400 mg) once daily</p>	<p>Orthographic similarities</p> <p>- Both names share letters in the same position that appear similar when scripted (‘Zoli-’ vs. ‘Xofi-’, ‘-za’ vs. ‘-go’)</p>	<p>Orthographic differences</p> <p>- Zolinza contains an additional letter (‘n’) in the middle of the name.</p> <p>Differing product characteristics</p> <p>- Dose: 2 to 4 tablets (200 mg to 400 mg) vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie</p> <p>- Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.</p>

No.	<p>Xofigo (Radium Ra 223 Dichloride Injection)</p> <p>1,000 kBq/mL (27 microcurie/mL)</p> <p>Usual Dose: 50 kBq/kg (3,000 kBq to 6,000 kBq) or 1.35 microcurie/kg (81 microcurie to 162 microcurie) every 4 weeks for 6 injections</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>
14.	<p>Zytopic (triamcinolone acetonide)</p> <p>0.1% Kit (cleanse and moisturizer)</p> <p>Usual Dose: Apply thin film to affected areas 2 to 3 times/day</p>	<p>Orthographic similarities</p> <p>- Both name share letters that appear similar when scripted (‘Z’ vs. ‘X’, ‘t’ vs. ‘f’, ‘p’ s. ‘g’)</p>	<p>Orthographic differences</p> <p>- Zytopic contains an additional downstroke letter (‘y’) in the second letter position.</p> <p>Differing product characteristics</p> <p>- Dose: Apply a thin film vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie</p> <p>- Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.</p>
15.	<p>Zomig (Zolmitriptan)</p> <p>2.5 mg, 5 mg tablets</p> <p>Usual Dose: 1 tablet once for headache attack, may repeat dose after 2 hours. Max 10 mg/24 hours</p> <p>5 mg nasal solution</p> <p>Usual Dose: 1 spray for acute migraine</p>	<p>Phonetic similarities</p> <p>- The first syllable in both names sounds identical (‘Zoh-’ vs. ‘Zoh-’)</p>	<p>Phonetic differences</p> <p>- The remaining syllables in the name differ (‘-mig’ vs. ‘-fee-go’)</p> <p>- The number of syllable differ (Zoh-mig vs. Zoh-fee-go)</p> <p>Differing product characteristics</p> <p>- Dose: 1 tablet or spray vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie</p> <p>- Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.</p>
16.	<p>Zovia (ethinyl estradiol and ethynodiol diacetate)</p> <p>0.035 mg/1 mg tablets</p> <p>0.05 mg/1 mg tablets</p> <p>Usual Dose: 1 tablet orally once daily</p>	<p>Phonetic similarities</p> <p>- The first 2 syllables in the names sound similar (Zoh-vee vs. Zoh-fee)</p>	<p>Phonetic differences</p> <p>- The last syllables sounds are different (‘-a’ vs. ‘-go’) mainly due to the consonant sound from the letter ‘g’.</p> <p>Differing product characteristics</p> <p>- Dose: 1 tablet vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie</p> <p>- Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.</p>

No.	<p>Xofigo (Radium Ra 223 Dichloride Injection)</p> <p>1,000 kBq/mL (27 microcurie/mL)</p> <p>Usual Dose: 50 kBq/kg (3,000 kBq to 6,000 kBq) or 1.35 microcurie/kg (81 microcurie to 162 microcurie) every 4 weeks for 6 injections</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>Xgeva (Denosumab)</p> <p>120 mg/1.7 mL</p> <p>Usual Dose: 120 mg subcutaneously every 4 weeks</p>	<p>Orthographic similarities</p> <ul style="list-style-type: none"> - Both names share identical initial letter ('X') - Both names share a letter that appears similar when scripted ('-a' vs. '-o') <p>Phonetic similarities</p> <ul style="list-style-type: none"> - no phonetic similarities <p>Overlapping product characteristics</p> <ul style="list-style-type: none"> - Similar patient population/indication: both products treat oncology patients with Bone Metastasis - Numerically similar dose: 120 mg vs. 120 microcurie - Dosage Form: Injection - Frequency of Administration: every 4 weeks 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Xgeva contains a downstroke letter ('g') in the second letter position. - Xofigo contains an upstroke letter ('f') in the middle of the name and a downstroke letter ('g') toward the end of the name. <p>Phonetic differences</p> <ul style="list-style-type: none"> - All the syllables differ (ex-gee-va vs. zoh-fee-go) <p>Differing product characteristics</p> <ul style="list-style-type: none"> - Dose: 120 mg vs. 3,000 kBq to 6,000 kBq - Although the doses may be numerically similar, the units of measure differ (mg vs. microcurie) - Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.

No.	<p>Xofigo (Radium Ra 223 Dichloride Injection)</p> <p>1,000 kBq/mL (27 microcurie/mL)</p> <p>Usual Dose: 50 kBq/kg (3,000 kBq to 6,000 kBq) or 1.35 microcurie/kg (81 microcurie to 162 microcurie) every 4 weeks for 6 injections</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.	<p>Xopenex (Levalbuterol HCl)</p> <p>0.31 mg, 0.63 mg, 1.25 mg inhalation solution</p> <p>Usual Dose: 1 vial in a nebulizer 3 times daily</p>	<p>Orthographic similarities</p> <ul style="list-style-type: none"> - Both names share identical letters in the same positions ('Xo-') <p>Phonetic similarities</p> <ul style="list-style-type: none"> - The first syllables sounds the same ('Zoh-') 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - The endings of the names differ ('-penex' vs. '-figo') <p>Phonetic differences</p> <ul style="list-style-type: none"> - The remaining syllables sound differently ('-pe-neks' vs. '-fee-go') <p>Differing product characteristics</p> <ul style="list-style-type: none"> - Dose: 1 vial (0.31 mg, 0.63 mg, 1.25 mg) vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie - Frequency of Administration: 3 times daily vs. every 4 weeks - Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.
19.	<p>Xtandi (Enzalutamide)</p> <p>40 mg capsule</p> <p>Dose: 2 to 4 capsules (80 mg to 160 mg) orally daily</p>	<p>Orthographic similarities</p> <ul style="list-style-type: none"> - Both names initial letter is identical ('X'). <p>Phonetic similarities</p> <ul style="list-style-type: none"> - none <p>Overlapping product characteristics</p> <ul style="list-style-type: none"> - Patient population: Prostate Cancer - Numerically Similar Dose: 80 mg, 160 mg vs. 80 microcurie, 160 microcurie 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - After the initial letter 'X', the remaining portion of the names differ ('-tandi' vs. '-ofigo') <p>Phonetic differences</p> <ul style="list-style-type: none"> - All syllables sound differently ('Ex-tahn-dee' vs. 'Zoh-fee-go') <p>Differing product characteristics</p> <ul style="list-style-type: none"> - Dose: 2 to 4 capsules (80 mg to 160 mg) vs. 3,000 kBq to 6,000 kBq - Although the doses may be numerically similar, the units of measure differ (mg vs. microcurie) - Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.

No.	<p>Xofigo (Radium Ra 223 Dichloride Injection)</p> <p>1,000 kBq/mL (27 microcurie/mL)</p> <p>Usual Dose: 50 kBq/kg (3,000 kBq to 6,000 kBq) or 1.35 microcurie/kg (81 microcurie to 162 microcurie) every 4 weeks for 6 injections</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>Zytiga (abiraterone)</p> <p>250 mg tablets</p> <p>Usual Dose: 1 to 4 tablets once orally daily</p>	<p>Orthographic similarities</p> <ul style="list-style-type: none"> - Both names share letters identical letters in similar positions ('-ig-'). - Both name share letters that appear similar when scripted ('t' vs. 'f', 'a' vs., 'o') <p>Phonetic similarities</p> <ul style="list-style-type: none"> - Both names contain 3 syllables - the first and third syllables sound similar ('Zy-' vs. 'Xoh-', '-ga' vs. '-go') <p>Overlapping product characteristics</p> <ul style="list-style-type: none"> - Identical Patient population: Prostate Cancer - Overlapping dose vs. Strength: Zytiga 1,000 mg dose vs. Xofigo 1,000 kBq/mL vial 	<p>Orthographic differences</p> <ul style="list-style-type: none"> - Zytiga contains the downstroke letter 'y' in the second position. <p>Phonetic differences</p> <ul style="list-style-type: none"> - The second syllable sounds differently ('-ti' vs. '-fee') <p>Differing product characteristics</p> <ul style="list-style-type: none"> - Dose: 1 to 4 capsules (250 mg to 1000 mg) vs. 3,000 kBq to 6,000 kBq or 81 microcurie to 162 microcurie. - Although the doses (Zytiga 1,000 mg) and strength (Xofigo 1,000 kBq/mL) may be numerically similar, the units of measure differ (mg vs. kBq). - Although the patient population is identical, the procurement, preparation, and administration of Xofigo is separate from Zytiga. - Setting of use: Xofigo is a radiopharmaceutical product that will be handled and managed by HCP that are authorized to manage radiopharmaceutical products.

Appendix G: Names previously reviewed in OSE Review 2011-1417 determined to have sufficient orthographic and/or phonetic differences

Proprietary Name	Active Ingredient	Similarity to Xofigo	Failure preventions
Phoslo	Ezogabine	Look	The pair have sufficient orthographic and/or phonetic differences
Xopenex	Levalbuterol HCl	Look and Sound	The pair have sufficient orthographic and/or phonetic differences
Zofran	Ondansetron	Look and Sound	The pair have sufficient orthographic and/or phonetic differences
Zometa	Zoledronic Acid	Look and Sound	The pair have sufficient orthographic and/or phonetic differences
Xigris	Drotrecogin Alfa (activated)	Look and Sound	The pair have sufficient orthographic and/or phonetic differences
Xomolix	Droperidol	Look and Sound	The pair have sufficient orthographic and/or phonetic differences
Zoloft	Sertraline	Look and Sound	The pair have sufficient orthographic and/or phonetic differences

Appendix H: Names previously reviewed in OSE Review 2011-1417 as determined to have risk of medication errors due to product confusion minimized by dissimilarity of the names and/or use in clinical practice for the reasons described.

Product name with potential for confusion	Similarity to Xofigo	Dosage Form/ Strength	Usual Dose	Differentiating product characteristics (Xofigo versus product)
Xofigo (radium 223 chloride)	N/A	Solution for Injection: 1,000 kBq/mL (0.03 mCi/mL) at date of calibration	50 kBq/kg intravenous bolus injection every 4 weeks for 6 injections	N/A
Exalgo (hydromorphone)	Sound	Tablet, extended-release: 8, 12, and 16 mg	8 to 64 mg by mouth every 24 hours	<p>Strength: 1,000 kBq/mL (0.03 mCi/mL) (single strength) vs. 8, 12, and 16 mg (multiple strength)</p> <p>Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. 1 tablet (8 mg) to 4 tablets (16 mg)</p> <p>Route of administration: intravenous bolus vs. oral</p> <p>Frequency: once every 4 weeks vs. every 24 hours</p> <p>Phonetic Differences: Xofigo is pronounced as ZOH-fee-go, the “fee” sound is not heard in Exalgo.</p>
Exforge (amlodipine/ valsartan)	Look or Sound (External Study)	Exforge Tablet: 5 mg/160 mg, 5 mg/320 mg, 10 mg/150 mg, and 10 mg/320 mg	10 mg/320 mg by mouth once daily	<p>Strength: 1,000 kBq/mL (0.03 mCi/mL) (single strength) vs. 5 mg/160 mg, 5 mg/320 mg, 10 mg/150 mg, and 10 mg/320 mg (multiple strength)</p> <p>Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. 1 tablet</p> <p>Route of administration: intravenous bolus vs. oral</p> <p>Frequency: once every 4 weeks vs. once daily</p>

Product name with potential for confusion	Similarity to Xofigo	Dosage Form/ Strength	Usual Dose	Differentiating product characteristics (Xofigo versus product)
Xofigo (radium 223 chloride)	N/A	Solution for Injection: 1,000 kBq/mL (0.03 mCi/mL) at date of calibration	50 kBq/kg intravenous bolus injection every 4 weeks for 6 injections	N/A
Exforge HCT (amlodipine/ valsartan/ hydrochlorothiazide)		Exforge HCT Tablet: 5 mg/160 mg/12.5 mg, 5 mg/160 mg/25 mg, 10 mg/160 mg/12.5 mg, 10 mg/160 mg/25 mg, 10 mg/320 mg/25 mg	10 mg/320 mg/25 mg by mouth once daily	Strength: 1,000 kBq/mL (0.03 mCi/mL) (single strength) vs. 5 mg/160 mg/12.5 mg, 5 mg/160 mg/25 mg, 10 mg/160 mg/12.5 mg, 10 mg/160 mg/25 mg, 10 mg/320 mg/25 mg (multiple strength) Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. 1 tablet Route of administration: intravenous bolus vs. oral Frequency: once every 4 weeks vs. once daily
Forfivo XL*** (bupropion HCl)	Look and Sound	Tablet, extended release: 450 mg	450 mg by mouth once daily	Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. 1 tablet Route of administration: intravenous bolus vs. oral Frequency: once every 4 weeks vs. once daily Orthographic Differences: Xofigo contains an additional down stroke letter “g” that is not seen in Forfivo XL

(b) (4)

Product name with potential for confusion	Similarity to Xofigo	Dosage Form/ Strength	Usual Dose	Differentiating product characteristics (Xofigo versus product)
Xofigo (radium 223 chloride)	N/A	Solution for Injection: 1,000 kBq/mL (0.03 mCi/mL) at date of calibration	50 kBq/kg intravenous bolus injection every 4 weeks for 6 injections	N/A
Keflex (cephalexin)	Look or Sound (External Study)	Capsule: 250 mg, 500 mg and 750 mg	250 to 1,000 mg by mouth every 6 hours	<p>Strength: 1,000 kBq/mL (0.03 mCi/mL) (single strength) vs. 250 mg, 500 mg and 750 mg (multiple strength)</p> <p>Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. 1 to 2 tablets</p> <p>Route of administration: intravenous bolus vs. oral</p> <p>Frequency: once every 4 weeks vs. every 6 hours</p> <p>Orthographic Differences: Keflex contains one additional upstroke letter “l” that is not seen in Xofigo; while Xofigo contains one down stroke letter “g” that is not seen in Keflex</p>
Kefzol (cefazolin) Foreign brand name for cefazoline. Generic versions available in the United States	Look or Sound (External Study)	In the US: Injection, powder for reconstitution: 500 mg, 1 g, 10 g, 20 g, 100 g, and 300 g	1 to 2 g intramuscular or intravenous injection or infusion every 8 hours	<p>Strength: 1,000 kBq/mL (0.03 mCi/mL) (single strength) vs. 500 mg, 1 g, 10 g, 20 g, 100 g, and 300 g (multiple strength)</p> <p>Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. 1 to 2 g</p> <p>Frequency: once every 4 weeks vs. every 8 hours</p> <p>Orthographic Differences: Kefzol contains one additional upstroke letter “l” at the end of the name, which is not seen in Xofigo</p>
		Injection, premixed iso-osmotic dextrose solution: 1 g	1 to 2 g intramuscular or intravenous injection or infusion every 8 hours	<p>Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. 1 to 2 g</p> <p>Frequency: once every 4 weeks vs. every 8 hours</p> <p>Orthographic Differences: same as above.</p>

Product name with potential for confusion	Similarity to Xofigo	Dosage Form/ Strength	Usual Dose	Differentiating product characteristics (Xofigo versus product)
Xofigo (radium 223 chloride)	N/A	Solution for Injection: 1,000 kBq/mL (0.03 mCi/mL) at date of calibration	50 kBq/kg intravenous bolus injection every 4 weeks for 6 injections	N/A
Viagra (sildenafil)	Look	Tablet: 25, 50, and 100 mg	50 mg by mouth one hour before sexual activity	Strength: 1,000 kBq/mL (0.03 mCi/mL) (single strength) vs. 25 mg, 50 mg, and 100 mg (multiple strength) Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. 1 tablet Route of administration: intravenous bolus vs. oral Frequency: once every 4 weeks vs. as needed Orthographic Differences: Xofigo contains one additional upstroke letter “f” that is not seen in Viagra
Vidaza (azacitidine)	Look	Injection, powder for suspension: 100 mg	75 mg/m ² /day subcutaneous or intravenous injection for 7 days, repeat every 4 weeks	Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. 130 mg (based on 1.73 m ² adult) Frequency: once every 4 weeks vs. daily for 7 days, repeat every 4 weeks
Xiaflex (collagenase clostridium histolyticum)	Look	Injection, powder for reconstitution: 0.9 mg	0.58 mg injection per Dupuytren’s cord. May re-inject cord up to 3 times at 4 week intervals.	Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. 0.58 mg Orthographic Differences: Xiaflex contains one additional upstroke letter “l” that is not seen in Xofigo; while Xofigo contains one down stroke letter “g” that is not seen in Xiaflex

Product name with potential for confusion	Similarity to Xofigo	Dosage Form/ Strength	Usual Dose	Differentiating product characteristics (Xofigo versus product)
Xofigo (radium 223 chloride)	N/A	Solution for Injection: 1,000 kBq/mL (0.03 mCi/mL) at date of calibration	50 kBq/kg intravenous bolus injection every 4 weeks for 6 injections	N/A
Xolair (omalizumab)	Look or Sound (External Study)	Injection, powder for reconstitution: 150 mg	Dose based on pretreatment IgE serum levels and body weight. Administered as a subcutaneous injection every 2 or 4 weeks. 150 mg subcutaneous injection every 4 weeks (based on 72 kg adult with serum IgE level greater than or equal to 30 to 100 international units/mL)	Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. 150 mg (based on 72 kg adult with serum IgE level greater than or equal to 30 to 100 international units/mL) Monitoring: none vs. serum IgE level Orthographic Differences: Xofigo contains one down stroke letter “g” that is not seen in Xolair
Xeloda (capecitabine)	Look	Tablet: 150 mg and 500 mg	1,000 to 1,250 mg/m ² by mouth twice daily for 2 weeks, every 21 days.	Strength: 1,000 kBq/mL (0.03 mCi/mL) (single strength) vs. 150 mg and 500 mg (multiple strength) Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. 2 to 4 tablets (1730 mg to 2152.5 mg based on 1.73 m ² adult, dispensed as the 500 mg strength tablet) Route of administration: intravenous bolus vs. oral Frequency: once every 4 weeks vs. twice daily for 2 weeks, every 21 days Orthographic Differences: Xeloda contains one additional upstroke letter “d” towards the end of the name, which is not seen in Xofigo; while Xofigo contains one down stroke letter “g” towards the end of the name that is not seen in Xeloda.

Product name with potential for confusion	Similarity to Xofigo	Dosage Form/ Strength	Usual Dose	Differentiating product characteristics (Xofigo versus product)
Xofigo (radium 223 chloride)	N/A	Solution for Injection: 1,000 kBq/mL (0.03 mCi/mL) at date of calibration	50 kBq/kg intravenous bolus injection every 4 weeks for 6 injections	N/A
Xolegel (ketoconazole)	Look	Gel, topical: 2%	Rub gently into the affected area once daily for 2 weeks.	Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. thin layer Route of administration: intravenous bolus vs. topical Frequency: once every 4 weeks vs. once daily Orthographic Differences: Xolegel contains one additional upstroke letter “l” at end of the name, which is not seen in Xofigo.
Zytiga (abiraterone acetate)	Look	Tablet: 250 mg	4 tablets by mouth once daily	Dose: 3600 kBq or 2.16 mCi (based on 72 kg adult) vs. 4 tablets Route of administration: intravenous bolus vs. oral Frequency: once every 4 weeks vs. once daily Orthographic Differences: Zytiga contains one additional down stroke letter “y” in the second position of the name, which is not seen in Xofigo.

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

/s/

JIBRIL ABDUS-SAMAD
03/29/2013

TODD D BRIDGES
03/29/2013

CAROL A HOLQUIST on behalf of KELLIE A TAYLOR
03/29/2013
Signing on behalf of Kellie Taylor

CAROL A HOLQUIST
03/29/2013