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RESEARCH**

APPLICATION NUMBER:

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PROPRIETARY NAME REVIEW(S)

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

Proprietary Name Review

Date: November 27, 2012

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

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Drug Name and Strength: Kynamro (Mipomersen) Injection, 200 mg/mL

Application Type/Number: NDA 203568

Applicant/Sponsor:  (b) (4)

OSE RCM #: 2012-2067

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Kynamro, from a safety and promotional perspective. This review responds to a September 6, 2012 request from Genzyme to reconsider the proposed proprietary name, Kynamro for NDA 206568.

1.1 REGULATORY HISTORY

The proprietary name, Kynamro for Mipomersen Sodium Injection, 200 mg/mL was initially submitted to IND 070969 and the proprietary name was found acceptable from a safety perspective by the Division of Medication Error Prevention and Analysis (DMEPA) in OSE# 2010-2325, dated March 24, 2011.

On April 12, 2012, the Applicant submitted a request for an assessment of the proposed proprietary name, Kynamro to NDA 203568. The proposed proprietary name, Kynamro, was found unacceptable due to orthographic similarities and overlapping product characteristics with a pending proposed proprietary name, (b) (4) in OSE# 2012-926, dated July 9, 2012. However, on August 14, 2012, the application (u) (4) was withdrawn, thus is no longer a concern for name confusion (See Appendix A).

On August 30, 2012, the Applicant was advised via electronic mail to resubmit the proposed proprietary name, Kynamro, since it is no longer vulnerable to name confusion based on previously identified concerns. The Applicant submitted a request for reconsideration of the proposed proprietary name, Kynamro on September 6, 2012. Since the last review was conducted less than 90 days from receipt of this submission, the review was abbreviated.

2 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 2012-926. 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 may have altered our previous conclusion regarding the acceptability of the proposed proprietary name. The searches of the databases yielded 2 new names (Tekamlo and (b) (4)), which were thought to look and sound similar to Kynamro and represent a potential source of drug name confusion. Failure mode and effects analysis was applied to determine if the proposed proprietary name could potentially be confused with Kynamro and lead to medication errors. This analysis determined that the name similarity between Kynamro and the identified names was unlikely to result in medication error for the reasons presented in Appendix A.

Additionally, DMEPA searched the 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 United States Adopted

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Names (USAN) stems in the proposed proprietary name, as of November 15, 2012. The Office of Prescription Drug Promotion (OPDP) re-reviewed the proposed name on September 13, 2012 and had no concerns regarding the proposed name from a promotional perspective.

3 CONCLUSIONS

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

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

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, Kynamro, and have concluded that this name is acceptable. However, if any of the proposed product characteristics as stated in your September 6, 2012 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. OSE Reviews:

1. OSE# 2012-926 Kynamro (Mipomersen Sodium) Injection Proprietary Name Review (NDA 203568), dated July 9, 2012
2. OSE# 2010-2325 Kynamro (Mipomersen Sodium) Injection Proprietary Name Review (IND 070969), dated March 24, 2011.

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.

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

Proprietary Name	Active Ingredient	Similarity to Kynamro	Failure Preventions
(b) (4)			

Appendix B: 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>Proposed name: Kynamro (Mipomersen Sodium) Dosage Form and Strength: Injection solution: 200 mg/mL Usual Dose: Inject 200 mg subcutaneously once weekly</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>Tekamlo (Aliskiren and Amlodipine) Dosage Form and Strength: Oral tablets: 150 mg/5 mg, 150 mg/10 mg, 300 mg/5 mg, 300 mg/10 mg Usual dose: <i>Initial therapy:</i> 150 mg/5 mg once daily; dose may be titrated at 2- to 4-week intervals; maximum recommended daily doses: 300 mg/10 mg <i>Add-on therapy:</i> Initiate at 150 mg/5 mg; dose may be titrated at 2- to 4-week intervals; maximum recommended daily doses: 300 mg/10 mg</p>	<p>Orthographic similarity: Both names contain the letter string ‘am’ and ends with the letter ‘o’ Phonetic similarity: Both names contain 3 syllables with a second syllable ‘am.’ The third syllables ‘ro’ and ‘lo’ sound phonetically similar when spoken.</p>	<p>Orthographic difference: The beginning letter strings ‘Kyn’ and ‘Tek’ appear orthographically different when scripted. In addition, Tekamlo contains an upstroke in position 6 which is absent in Kynamro, giving the names different shapes. Phonetic difference: The beginning syllable ‘Kyn’ and ‘Tek’ sound phonetically different when spoken. Strength: Single vs. multiple. Kynamro is available in single strength and may be omitted from a prescription vs. an order for Tekamlo will require a strength as it is available in multiple strengths. Frequency: Kynamro is prescribed once weekly vs. Tekamlo is prescribed once daily. Dose: Inject 200 mg vs. Take 1 tablet</p>

No.	<p>Proposed name: Kynamro (Mipomersen Sodium)</p> <p>Dosage Form and Strength: Injection solution: 200 mg/mL</p> <p>Usual Dose: Inject 200 mg subcutaneously once weekly</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>
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(b) (4)

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/s/

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11/27/2012

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11/27/2012

**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 6, 2012

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

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Drug Name and Strength(s): Kynamro (Mipomersen) Injection, 200 mg/mL

Application Type/Number: NDA 203568

Applicant/Sponsor: (b) (4)

OSE RCM #: 2012-1024

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Kynamro, 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 submitted a request for an assessment of the proposed proprietary name, Kynamro for Mipomersen Sodium Injection, 200 mg/mL in NDA 203568 on April 12, 2012. The name proprietary name, Kynamro was initially submitted to IND 070969 and the proprietary name was found acceptable from a safety perspective by the Division of Medication Error Prevention and Analysis (DMEPA) in OSE# 2010-2325, dated March 24, 2011.

1.2 PRODUCT INFORMATION

The following product information is provided in the April 12, 2012 proprietary name submission.

- Active Ingredient: Mipomersen Sodium
- Indication of Use: an adjunct to maximally tolerated lipid-lowering medications and diet to reduce LDL-C, apo B, TC, non-HDL-C, (b) (4) levels in patients with homozygous familial hypercholesterolemia (HoFH) (b) (4)
- Route of Administration: Subcutaneous
- Dosage Form: Injection solution
- Strength: 200 mg/mL
- Dose and Frequency: Once weekly
- How Supplied: Pre-filled syringe are packed individually into trays. Syringes in trays are placed in cartons with prescribing information. The cartons provide protection from light. Vials are packed individually in cartons with prescribing information. The cartons provide protection from light
- Storage: Between 2°C to 8°C. Protect from light.
- Container and Closure Systems: *Vials*: (b) (4) 2 mL, clear glass vials with (b) (4) rubber stoppers (b) (4)
The vials are capped with (b) (4) flip-off caps.
Prefilled syringe: (b) (4) 1 mL, (b) (4) clear glass syringes with (b) (4) needles and needle shields with (b) (4) rubber plunger stoppers (b) (4)
Syringes are assembled with a plunger rod and a needle shield safety device.

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 (DMEP) concurred with the findings of OPDP's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

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

2.2.1 United States Adopted Names (USAN) SEARCH

The May 29, 2012 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, Kynamro, was not derived from any one particular concept and has no intended 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

Thirty practitioners participated in DMEPA's prescription studies. The interpretations did not overlap with or appear or sound similar to any currently marketed products. Two of the 10 inpatient participants responded correctly and the 2 most common misinterpretations occurred with 2 participants misinterpreting the letter 'a' for 'u' in 'KynAmro' and 2 participants misinterpreting the letter 'r' for 'm' and 'v' in 'KynamRo.' None of the 13 voice participants responded correctly and the most common misinterpretation occurred with 2 participants misinterpreting the letter 'K' for 'Ch' in 'Kynamro.' Four out of 10 outpatient participants responded correctly and the most common misinterpretation occurred with 2 participants misinterpreting the letter 'n' for 'm' in 'KyNamro.' See Appendix C for the complete listing of interpretation from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines

In response to the OSE, May 3, 2012 e-mail, the Division of Metabolism and Endocrinology Products (DMEP) did not forward any comments or concerns relating to the proposed name at the initial phase of the proprietary name review.

2.2.6 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, Kynamro. Table 1 lists the names with

orthographic, phonetic, or spelling similarity to the proposed proprietary name, Kynamro identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines. Table 1 also includes the names identified from the FDA Prescription Simulation or by (b) (4) not identified by DMEPA and requires further evaluation.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD, Other Disciplines, FDA Name Simulation Studies, and External Name Study)

Look Similar					
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
Xopenex	FDA	Hycomine	FDA	Xyrem	FDA
Rinnovi	FDA	Hysone	FDA	Kineret	FDA
Hyamine	FDA	(b) (4)	FDA	Hyzaar	FDA
Rapamune	FDA	Regranex	FDA	Synvisc	FDA
Krystexxa	FDA	Vyvanse	FDA	Rynesa 12S	FDA
Ku-zyme	FDA	Rynatuss	FDA	Rynatan	FDA
Minipress	FDA	Kynapid***	FDA	Heparin	FDA/External
Kinrix	FDA	Lyxumia***	FDA	Kariva	FDA/External
Kybernin P	FDA	Ryna-mine	FDA	Humira	FDA/External
(b) (4)	FDA	Kinevac	FDA	Glynase	FDA/External
Kanamycin	FDA	Kinerase	FDA	Humalog	FDA/External
Ketoconazole	External				
Sound Similar					
Avapro	External	Kytril	External		
Look and Sound Similar					
Kynamro	FDA	Lexapro	External		

Our analysis of the 38 names contained in Table 1 considered the information obtained in the previous sections along with their product characteristics. We determined 37 of the 38 total number of names will not pose a risk for confusion as described in Appendix D and E.

However, the proposed name could be confused with (b) (4), a name that is pending review in the Agency. The rationale for the risk of confusion is described below.

The proposed proprietary name, Kynamro, is orthographically similar to and shares product characteristics with (b) (4). Since (b) (4) is not approved, DMEPA cannot provide specifics on the proposed similarity of this name pair to the Applicant,

(b) (4)

The similarities of the name pair, in combination with the overlapping product characteristics, increase the potential for errors to occur in the medication use system resulting in wrong drug medication errors.

(b) (4)

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2.2.7 Communication of DMEPA's Final Decision to Other Disciplines

DMEPA communicated our findings to the Division of Metabolism and Endocrinology Products via e-mail on June 15, 2012. 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 July 6, 2012 they stated no additional concerns with the proposed proprietary name, Kynamro.

3 CONCLUSIONS

The proposed proprietary name is acceptable from a promotional perspective but not acceptable from a safety perspective. The proposed name is vulnerable to name confusion with (b) (4). Therefore, the decision to deny the name will be communicated to the Applicant via letter (See *Section 3.1*).

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, Kynamro, and have concluded that it is vulnerable to name confusion that could lead to medication errors with a pending proposed proprietary name due to orthographic similarity and shared product characteristics. Therefore, at this time, the acceptability of the proposed proprietary name, Kynamro, is dependent upon which application is approved first. If Kynamro is approved first, we will advise the second product to seek an alternative name. If the second name application is approved prior to your application then you will be requested to submit another name.

If you wish to withdraw Kynamro to avoid the potential confusion with the other pending name and submit an alternate name for review, please submit a request for withdrawal and submit a new proprietary name for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Margarita Tossa, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-4053. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Kati Johnson, at (301) 796-1234.

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.

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).

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>
	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

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

Look-alike			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 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:

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

“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.

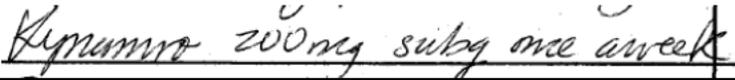
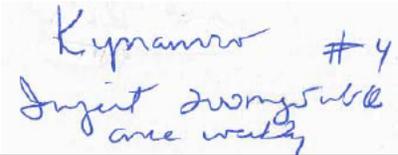
Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors 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 with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Kynamro	Scripted may appear as	Spoken may be interpreted as
‘K’ ‘k’	R, X, x, h, la	C, Qu, Que, Q
Lowercase ‘y’	f, p, u, v, x, Z	e, i, u
lowercase ‘n’	M, u, x, r, h, s	dn, gn, kn, mn, pn
lowercase ‘a’	El, ci, cl, d, o, u, e	Any vowel
lowercase ‘m’	Rn, mn, n, v, w, wi, vi, onc, z	
Lowercase ‘r’	s, n, e, v	
lowercase ‘o’	a, c, e, u	Oh

Appendix C: Prescription Simulation Samples and Results

Figure 1. Kynamro Study (Conducted on May 11, 2012)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> 	<p>Kynamro</p> <p>Inject 200 mg subcutaneously once a week</p>
<p><u>Outpatient Prescription:</u></p> 	

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

84 People Received Study

30 People Responded

Total	10	13	10	30
INTERPRETATION	INPATIENT	VOICE	OUTPATIENT	TOTAL
CAINAMERILE	0	1	0	1
CHYNAMRO	0	2	0	2
HYNAMORAL HF	0	1	0	1
KINAMERAL	0	1	0	1
KINAMERO	0	1	0	1
KINAMEROL	0	1	0	1
KIPSUMRO	1	0	0	1
KYMAMRO	0	0	2	2
KYMARRO	0	0	1	1
KYNAMERIL	0	1	0	1
KYNAMIRO	0	0	1	1
KYNAMMO	1	0	0	1

KYNAMRIL	0	1	0	1
KYNAMRO	2	0	4	6
KYNAMROL	0	1	0	1
KYNAMURAL	0	1	0	1
KYNAMVO	1	0	0	1
KYNANNO	1	0	0	1
KYNUMRO	2	0	0	2
LYNAMRO	1	0	0	1
LYNUMUVO	1	0	0	1
PINAMRAL	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 Kynamro	Failure preventions
<i>Kynamro</i> ***	(Mipomersen Sodium)	Orthographic	Subject of this review
<i>Xopenex</i>	Levalbuterol Tartrate	Orthographic	The pair has sufficient orthographic differences
<i>Rimovi</i>	Urea 50%	Orthographic	The pair has sufficient orthographic differences
<i>Humira</i>	Adalimumab	Orthographic	The pair has sufficient orthographic differences
<i>Glyrase</i>	Glyburide Micronized	Orthographic	The pair has sufficient orthographic differences
<i>Kariva</i>	Ethinyl Estradiol and Desogestrel	Orthographic	The pair has sufficient orthographic differences
<i>Humalog</i>	Insulin Lispro	Orthographic	The pair has sufficient orthographic differences
<i>Krystexxa</i>	Pegloticase	Orthographic	The pair has sufficient orthographic differences

<i>Ku-zyme</i>	Pancrealipase	Orthographic	The pair has sufficient orthographic differences
Minipress	<i>Prazocin</i>	Orthographic	The pair has sufficient orthographic differences
<i>Kinrix</i>	diphtheria, tetanus, inactivated pertussis toxin, type 1 poliovirus antigen, type 2 and type 3 poliovirus	Orthographic	The pair has sufficient orthographic differences
N/A	<i>Ketoconazole</i>	Orthographic	The pair has sufficient orthographic differences
<i>Kytril</i>	Granisetron	Phonetic	The pair has sufficient phonetic differences
<i>Lexapro</i>	Escitalopram oxalate	Orthographic and Phonetic	The pair has sufficient orthographic and phonetic differences
<i>Kybernin P</i>	Antithrombin III (human) concentrate IV	Orthographic	Orphan drug. No pending NDA or commercial IND within the agency
(b) (4)			
<i>Hyamine</i>	Benzethonium chloride	Orthographic	Name identified in Redbook database. Unable to find product characteristics in commonly used drug databases.
<i>Hycomine</i>	Hydrocodone Bitartrate, Phenylpropanolamine HCl	Orthographic	Name identified in FDA database. Unable to find product characteristics in commonly used drug databases. Withdrawn Pending FR Notice, March 27, 2009.
<i>Hyson</i>	Hydrocortisone	Orthographic	International product marketed in Pakistan

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>Proposed name: Kynamro (Mipomersen Sodium) Dosage Form and Strength: Injection solution: 200 mg/mL Usual Dose: Inject 200 mg subcutaneously once weekly</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>
<p>Regranex (Becaplermin) Dosage Form and Strength: Topical gel: 1 % Usual dose: Apply a sufficient amount of gel once daily</p>	<p>Orthographic similarity: The letters ‘K’ and ‘R’ and the letter strings ‘nam’ and ‘ran’ appear orthographically similar when scripted. In addition, both names contain a downstroke ‘y’ and ‘g’ in similar positions. Strength: Both are available as single strengths and may be omitted during prescription writing. **Preliminary usage data shows “as directed” has been used.</p>	<p>Orthographic difference: The ending letter string ‘ro’ and ‘ex’ appear orthographically different when scripted. Dose: Inject 200 mg vs. apply sufficient amount or as directed. Frequency: Kynamro is prescribed once weekly vs. Regranex is prescribed once daily.</p>

<p>Proposed name: Kynamro (Mipomersen Sodium)</p> <p>Dosage Form and Strength: Injection solution: 200 mg/mL</p> <p>Usual Dose: Inject 200 mg subcutaneously once weekly</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>Vyvanse (Lisdexamfetamine Dimesylate)</p> <p>Dosage Form and Strength: Oral Capsules: 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg</p> <p>Usual dose: Initially, take 30 mg by mouth once daily in the morning. If necessary, dosage increases may be made in increments of 10 or 20 mg per day at weekly intervals. Do not exceed 70 mg/ day.</p>	<p>Orthographic similarity: The letter strings ‘ynamro’ and ‘yvanse’ appear orthographically similar when scripted. In addition, both names contain the same number of letters and are similarly shaped.</p> <p>Strength: There is numerical overlap between the strengths (200 mg vs. 20 mg)</p> <p>Dose: There is numerical overlap between the doses (200 mg vs. 20 mg)</p>	<p>Orthographic difference: The letter ‘K’ and ‘V’ appear orthographically different when scripted.</p> <p>Frequency: Kynamro is prescribed once weekly vs. Vyvanse is prescribed once daily</p>

<p>Proposed name: Kynamro (Mipomersen Sodium) Dosage Form and Strength: Injection solution: 200 mg/mL Usual Dose: Inject 200 mg subcutaneously once weekly</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>
<p>Heparin Dosage Form and Strength: Premixed Infusion Solution: 25,000 units/250 ml 25,000 units/500 mL 12,500 units/250 mL 20,000 units/500 mL 25,000 units/250 mL 25,000 units/500 mL Injection Solution: 1000 units/ml 5000 units/mL 25,000 units/mL Usual Dose: Dose varies on patient weight and indication and ranges from 1000 units to 20,000 units every 8 to 12 hours or as a continuous infusion.</p>	<p>Orthographic Similarities: The letter ‘K’ and ‘H’ and the letter string ‘y’ and ‘ep’ appear orthographically similar when scripted. Dosage form and route of administration: Both are available as injection solution given subcutaneously Dose: There is numerical overlap between the doses. (200 mg vs. 2000 mg)</p>	<p>Orthographic difference: The ending letter strings ‘namro’ and ‘arin’ appear orthographically different when scripted. Frequency: Kynamro is prescribed once weekly vs. Heparin is prescribed as a continuous infusion or every 8 to 12 hours as a subcutaneous injection</p>

<p>Proposed name: Kynamro (Mipomersen Sodium) Dosage Form and Strength: Injection solution: 200 mg/mL Usual Dose: Inject 200 mg subcutaneously once weekly</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>
<p>Kynapid*** (Vernakalant HCl)</p> <p>(b) (4)</p>	<p>Orthographic similarity: Both names begin with the letter string 'Kyna'</p> <p>Dosage form and route of administration: Both are available as injection solution for parenteral use</p> <p>(b) (4)</p>	<p>Orthographic difference: Kynapid contains an additional downstroke 'p' in the fifth position and an upstroke 'd' in the last position which is absent in Kynamro giving the names different shapes.</p> <p>(b) (4)</p>
<p>(Kynapid*** (b) (4) OSE OSE# 2008-16, dated January 9, 2008 is currently under Approvable status)</p>		

<p>Proposed name: Kynamro (Mipomersen Sodium)</p> <p>Dosage Form and Strength: Injection solution: 200 mg/mL</p> <p>Usual Dose: Inject 200 mg subcutaneously once weekly</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>Ryna-Mine Pediatric (Chlorpheniramine, Phenylephrine, Pyrilamine)</p> <p>Dosage Form and Strength: Oral suspension: 2 mg/5 mg/12.5 mg per 5 mL</p> <p>Usual dose: Greater than 6 years- 5 to 10 mL every 12 hours; 2 to 6 years- 2.5 to 5 mL every 12 h; Less than 2 years- titrate dose individually</p>	<p>Orthographic similarities: The letters ‘K’ and ‘R’ appear orthographically similar when scripted and both names contain the letter string ‘ynam’ in the same position.</p> <p>Strength: Both are available in single strength and may be omitted from a prescription.</p>	<p>Frequency: Kynamro is prescribed once weekly vs. Ryna-mine is prescribed every 12 hours.</p> <p>Dose: 200 mg vs. 2.5 to 10 mL</p>

<p>Proposed name: Kynamro (Mipomersen Sodium) Dosage Form and Strength: Injection solution: 200 mg/mL Usual Dose: Inject 200 mg subcutaneously once weekly</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>
<p>Kinevac (Sincalide) Dosage Form and Strength: Injection solution, reconstituted: 5 mcg Usual dose: Average dose is based on a 72 kg adult: Gallbladder Contraction Stimulation and Pancreatic Secretion Testing: Intravenous: 0.02 mcg/kg (1.44 mcg) over 30 to 60 seconds. Intramuscular: 0.1 mcg/kg (7.2 mcg) over 30 to 60 seconds.</p>	<p>Orthographic similarities: Both names begin the letter K and the letter strings ‘nam’ and ‘nev’ appear orthographically similar when scripted. Strength: Both Kynamro and Kinevac are available as single strengths and may be omitted from a prescription. Dosage form and route of administration: Both are available as injection solution for parenteral use.</p>	<p>Orthographic similarities: Kynamro contains a downstroke ‘y’ in the second position which is absent in Kinevac giving the names different shapes. In addition, the ending letter strings ‘ro’ and ‘ac’ appear orthographically different when scripted. Frequency: Kynamro is prescribed once weekly vs. Kinevac is prescribed once.</p>

<p>Proposed name: Kynamro (Mipomersen Sodium)</p> <p>Dosage Form and Strength: Injection solution: 200 mg/mL</p> <p>Usual Dose: Inject 200 mg subcutaneously once weekly</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>Kinerase (Proprietary name for a line of over the counter skin care products)</p> <p>Dosage Form and Strength: Topical cream and lotion: 0.1% and 0.125%</p> <p>Usual dose: Use as directed</p>	<p>Orthographic similarity: Both names begin with the letter 'K' and the letter strings 'nerase' and 'namro' appear orthographically similar when scripted.</p>	<p>Strength: Single vs. multiple. Kynamro is available in single strength and may be omitted from a prescription vs. an order for Kinerase will require a strength as it is available in multiple strengths. There is no numerical overlap in strengths. In addition, the units of strength also differ (<i>mg vs. %</i>).</p> <p>Dosage form and route of administration: Kynamro is available as an injection solution vs. Kinerase is available as either a cream or lotion.</p>

<p>Proposed name: Kynamro (Mipomersen Sodium)</p> <p>Dosage Form and Strength: Injection solution: 200 mg/mL</p> <p>Usual Dose: Inject 200 mg subcutaneously once weekly</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>Kanamycin (Kanamycin Sulfate)</p> <p>Dosage Form and Strength: Injection Solution: 333 mg/mL</p> <p>Usual dose: Adults: Intramuscular and Intravenous: 15 mg/kg/day in 2 or 3 equally divided dosages administered at equally divided intervals (i.e., 7.5 mg/kg every 12 hours). Average dose based on 72 kg: 540 mg every 12 hours.</p> <p>Children: Intramuscular and Intravenous: Dose based on 1 to 5 kg: 7.5 mg to 37.5 mg every 12 hours</p>	<p>Orthographic similarities: Both names begin the letter K and contain the letter strings ‘nam’ in similar positions.</p> <p>Strength: Both Kynamro and Kanamycin are available as single strengths and may be omitted from a prescription.</p> <p>Dosage form and route of administration: Both are available as injection solution for parenteral use.</p>	<p>Orthographic similarities: Kynamro contains a downstroke ‘y’ in the second position vs. Kanamycin contains a downstroke ‘y’ in the sixth position giving the names different shapes. In addition, the ending letter strings ‘ro’ and ‘cin’ appear orthographically different when scripted.</p> <p>Frequency: Kynamro is prescribed once weekly vs. Kanamycin is prescribed every 12 hours.</p>

<p>Proposed name: Kynamro (Mipomersen Sodium) Dosage Form and Strength: Injection solution: 200 mg/mL Usual Dose: Inject 200 mg subcutaneously once weekly</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>
<p>Rynesa 12S (Phenylephrine Tannate, Pyrilamine Tannate), Dosage Form and Strength: Oral Suspension 5 mg/30 mg per 5 ml (Rynesa 12S is discontinued but different generics are available in the market) Usual dose: Take 5 to 10 ml by mouth every 12 hours.</p>	<p>Orthographic similarity: The letters ‘Kyna’ and ‘Ryne’ appear orthographically similar when scripted. Strength: Both Kynamro and Rynesa 12S are available in single strength and may be omitted from a prescription</p>	<p>Orthographic difference: The ending letter strings ‘mro’ and ‘sa’ appear orthographically different when scripted. If included, the modifier ‘12S’ can help distinguish the two names. Frequency: Kynamro is prescribed once weekly vs. Rynesa 12S is prescribed every 12 hours. Dose: 200 mg vs. 5 to 10 mL</p>
<p>Xyrem (Sodium Oxabate) Dosage Form and Strength: Oral solution: 500 mg/mL Usual dose: 6 to 9 g/night. Initial dosage: 4.5 g/night divided into 2 equal doses of 2.25 g. The first dose is taken while in bed, and the second dose is taken 2.5 to 4 hours later.</p>	<p>Orthographic similarity: The letter strings ‘Kynam’ and ‘Xyrem’ appear orthographically similar when scripted. Strength: Both Kynamro and Xyrem are available in single strengths and may be omitted from prescription.</p>	<p>Orthographic difference: Kynamro (7 letters) appear orthographically longer than Xyrem (5 letters) when scripted. In addition, the ending letter strings ‘mro’ and ‘m’ appear orthographically different when scripted. Frequency: Kynamro is prescribed once weekly vs. Xyrem is prescribed every at bedtime.</p>

<p>Proposed name: Kynamro (Mipomersen Sodium)</p> <p>Dosage Form and Strength: Injection solution: 200 mg/mL</p> <p>Usual Dose: Inject 200 mg subcutaneously once weekly</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>Kineret (Anakinra)</p> <p>Dosage Form and Strength: Subcutaneous solution: 100 mg/0.67 mL</p> <p>Usual dose: Inject 100 mg daily suncutaneously</p>	<p>Orthographic similarity: Both names begin with the letter ‘K’ and the letter strings ‘nam’ and ‘ner’ appear orthographically similar when scripted.</p> <p>Strength: Both are available as single strengths and may be omitted.</p> <p>Dosage form and route of administration: Both are available as injection solution given subcutaneously.</p>	<p>Orthographic difference: Kynamro contains a downstroke ‘y’ in the second position which is absent in Kineret. In addition, Kineret contains a cross stroke ‘t’ at the end of the name which is absent in Kynamro giving the names different shapes. In addition, the ending letter strings ‘amro’ and ‘eret’ appear orthographically different when scripted.</p> <p>Frequency: Kynamro is prescribed once weekly vs. Kineret is prescribed once daily</p>

<p>Proposed name: Kynamro (Mipomersen Sodium) Dosage Form and Strength: Injection solution: 200 mg/mL Usual Dose: Inject 200 mg subcutaneously once weekly</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>
<p>Hyzaar (Losartan and Hydrochlorothiazide) Dosage Form and Strength: Oral tablets: 50 mg/12.5 mg; 100 mg/12.5 mg, 100 mg/25 mg Usual dose: Take one tablet by mouth daily</p>	<p>Orthographic similarity: The letter strings 'Kyna' and 'Hyza' and appear orthographically similar when scripted.</p>	<p>Orthographic difference: The ending letter strings 'mro' and 'aar' appear orthographically different when scripted. Frequency: Kynamro is prescribed once weekly vs. Hyzaar is prescribed once. Strength: Single vs. multiple. Kynamro is available in single strength and may be omitted from a prescription vs. an order for Hyzaar will require a strength as it is available in multiple strengths. There is no numerical overlap in strengths. Dose: 200 mg vs. One tablet</p>

<p>Proposed name: Kynamro (Mipomersen Sodium)</p> <p>Dosage Form and Strength: Injection solution: 200 mg/mL</p> <p>Usual Dose: Inject 200 mg subcutaneously once weekly</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>Synvisc (Hyaluronate)</p> <p>Dosage Form and Strength: Intra-articular injection solution: 8 mg/mL</p> <p>Usual dose: Inject 16 mg (2 mL) once weekly for 3 weeks Inject 48 mg (6 mL) once</p>	<p>Orthographic similarity: Both names contain the letter string ‘yn’ in the same position.</p> <p>Strength: Both are available as single strengths and may be omitted during prescription writing.</p> <p>Dosage form and route of administration: Both are available as injection solution for parenteral use.</p> <p>Frequency: Both may be prescribed once weekly</p>	<p>Orthographic difference: The letter ‘K’ and ‘S’ and the ending letter strings ‘amro’ and ‘visc’ appear orthographically different when scripted.</p>

<p>Proposed name: Kynamro (Mipomersen Sodium)</p> <p>Dosage Form and Strength: Injection solution: 200 mg/mL</p> <p>Usual Dose: Inject 200 mg subcutaneously once weekly</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>Avapro (Irbesartan)</p> <p>Dosage Form and Strength: Oral tablets: 75 mg, 150 mg, 300 mg</p> <p>Usual dose: Take one tablet by mouth once daily</p>	<p>Phonetic Similarity: Both names contain three syllables and the last syllable ‘roh’ sound phonetically similar when spoken.</p>	<p>Phonetic Difference: The first syllable ‘Kye’ and ‘Uh’ and second syllable ‘nam’ and ‘vuh’ sound phonetically different when spoken.</p> <p>Strength: Single vs. multiple. Kynamro is available in single strength and may be omitted from a prescription vs. an order for Avapro will require a strength as it is available in multiple strengths. There is no numerical overlap in strengths.</p> <p>Frequency: Kynamro is prescribed once weekly vs. Avapro is prescribed once daily</p> <p>Dose: Inject 200 mg vs. One tablet</p>

<p>Proposed name: Kynamro (Mipomersen Sodium) Dosage Form and Strength: Injection solution: 200 mg/mL Usual Dose: Inject 200 mg subcutaneously once weekly</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>
<p>Rynatan (Chlorpheniramine Tannate, Phenylephrine Tannate) Dosage Form and Strength: Chewable tablets: 4.5 mg/5 mg Extended-release capsules: 4 mg/20 mg Usual dose: Children greater than 6 years: 1 to 2 chewable tablets by mouth every 12 hours. Children 2 to 6 years: One-half to one chewable tablet by mouth every 12 hours Extended-release capsules: Adults and Adolescents: 2 capsules by mouth every 12 hours, not to exceed 2 doses in 24 hours. Children 6 to 12 years: 1 capsule every 12 hours, not to exceed 2 doses in 24 hours.</p>	<p>Orthographic similarities: The letters ‘K’ and ‘R’ appear orthographically similar when scripted and both names contain the letter string ‘yna’ in the same position.</p>	<p>Orthographic similarities: Rynatan contains a cross stroke ‘t’ in the fifth position which is absent in Kynamro giving the names different shapes. In addition, the ending letter strings ‘mro’ and ‘tan’ appear orthographically different when scripted. Strength: Single vs. multiple. Kynamro is available in single strength and may be omitted from a prescription vs. an order for Rynatan will require a strength as it is available in multiple strengths. There is no numerical overlap in strengths. Frequency: Kynamro is prescribed once weekly vs. Rynatan is prescribed every 12 hours. Dosage form: Kynamro is available as an injection solution vs. Rynatan is available in chewable tablets, or extended-release capsules which need to be specified for a complete prescription. Dose: Inject 200 mg vs. Take one tablet or capsule</p>

<p>Proposed name: Kynamro (Mipomersen Sodium) Dosage Form and Strength: Injection solution: 200 mg/mL Usual Dose: Inject 200 mg subcutaneously once weekly</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>
<p>Rynatuss (Carbetapentane Tannate, Chlorpheniramine Tannate, Ephedrine Tannate, Phenylephrine Tannate) Dosage Form and Strength: Oral Tablets: Single strength- 60 mg/5 mg/10 mg/10 mg Usual dose: 1 to 2 tablets by mouth every 12 hours</p> <p>Rynatuss Pediatric Suspension (Carbetapentane Tannate, Chlorpheniramine Tannate, Ephedrine Tannate, Phenylephrine Tannate) Dosage Form and Strength: Oral Suspension: 30 mg/4 mg/5 mg/5 mg per 5 ml (Although Rynatuss Pediatric suspension is discontinued, other generics are available) Usual dose: Children 6 to 12 years: 5 to 10 mL by mouth every 12 hours. Children 2 to 6 years: 2.5 to 5 ml by mouth every 12 hours.</p>	<p>Orthographic similarities: The letters ‘K’ and ‘R’ appear orthographically similar when scripted and both names contain the letter string ‘yna’ in the same position.</p>	<p>Orthographic similarities: Rynatuss contains a cross stroke ‘t’ in the fifth position which is absent in Kynamro giving the names different shapes. In addition, the ending letter strings ‘mro’ and ‘tuss’ appear orthographically different when scripted.</p> <p>Frequency: Kynamro is prescribed once weekly vs. Rynatuss is prescribed every 12 hours.</p> <p>Dosage form: Kynamro is available as an injection solution vs. Rynatuss is available in tablets or pediatric suspension which needs to be specified for a complete prescription.</p> <p>Dose: Inject 200 mg vs. Take 1 to 2 tablets or 5 to 10 mL</p>

<p>Proposed name: Kynamro (Mipomersen Sodium) Dosage Form and Strength: Injection solution: 200 mg/mL Usual Dose: Inject 200 mg subcutaneously once weekly</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>
<p>Rapamune (Sirolimus) Dosage Form and Strength: Oral Tablet: 0.5 mg, 1 mg, 2 mg Usual dose: Low-to-moderate immunologic risk renal transplant patients: Oral: Less than 40 kg: Loading dose: 3 mg/m² on day 1, followed by maintenance dosing of 1 mg/m² once daily. Greater than or equal to 40 kg: Loading dose: 6 mg on day 1; maintenance: 2 mg once daily High immunologic risk renal transplant patients: Oral: Loading dose: Up to 15 mg on day 1; maintenance: 5 mg per day; obtain trough concentration between days 5 to 7 and adjust. Hepatic impairment: Mild to moderate hepatic impairment: reduce maintenance dose by approximately 33%. Severe hepatic impairment: reduce maintenance dose by approximately 50%.</p>	<p>Orthographic similarity: The letter s ‘K’ and ‘R’ and the letter strings ‘amro’ and ‘amune’ appear orthographically similar when scripted. In addition, both names contain a downstroke ‘y’ and ‘p’ in similar positions.</p>	<p>Strength: Single vs. multiple. Kynamro is available in single strength and may be omitted from a prescription vs. an order for Rapamune will require a strength as it is available in multiple strengths. There is no numerical overlap in strengths. Frequency: Kynamro is prescribed once weekly vs. Rapamune is prescribed once daily Dose: 200 mg vs. One tablet</p>

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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
07/06/2012

YELENA L MASLOV
07/06/2012

CAROL A HOLQUIST on behalf of KELLIE A TAYLOR
07/06/2012
Acting on behalf of Kellie Taylor

CAROL A HOLQUIST
07/06/2012